The Journal
OF THE KANSAS MEDICAL SOCIETY

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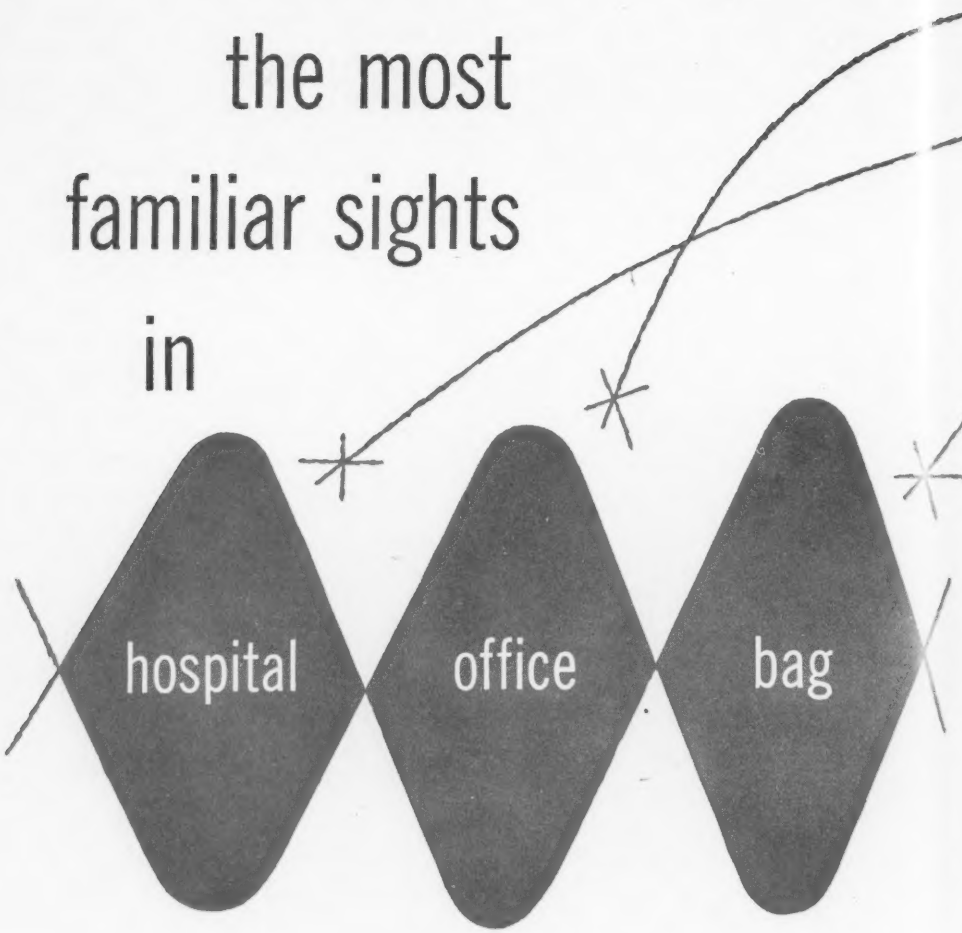

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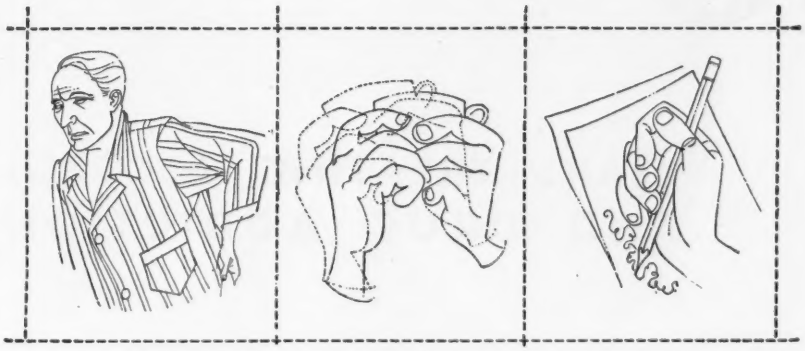

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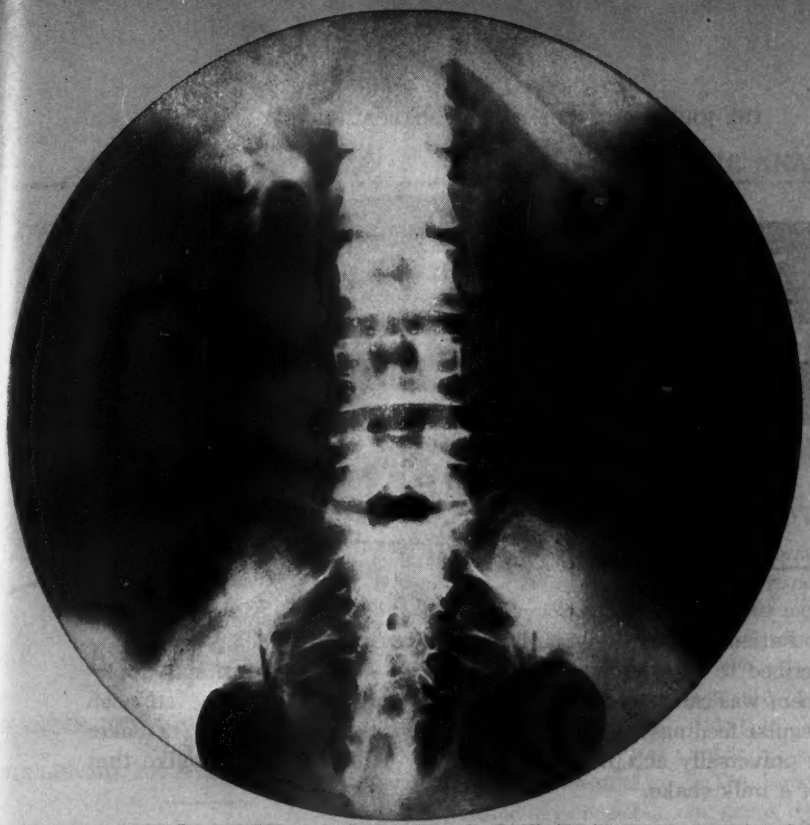

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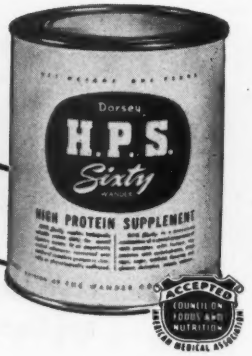

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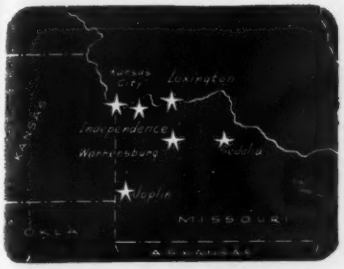

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Custer, R. Philip, *An Atlas of the Blood and Bone Marrow*, W. B. Saunders Co., 1949, p. 28.

Pathologically Speaking

HEMOGLOBIN DETERMINATION

THE estimation of hemoglobin constitutes a basic laboratory procedure of utmost importance. Hemoglobin, an iron-containing protein, is a vital agent in maintaining life, for it is the means whereby all cells are supplied with oxygen necessary to carry on various metabolic reactions.

The estimation of hemoglobin is a very important laboratory procedure as it varies widely in disease. The procedure is of value in routine survey, in disease, in following response to therapy, and it is a "must" prior to surgical intervention with general anesthesia.

The laboratory determination of hemoglobin is usually done on a colorimetric basis as spectroscopic and chemical procedures are for research laboratories. The colorimetric estimation offers several problems which the clinician should appreciate from clinical appraisal of reports.

There are numerous methods available for estimations, however, and the normal values for various methods will vary from 13.0 to 18.0 grams per 100 ml. Hence normal value for 100% is at variance and will depend upon the method used. The per cent of error will vary as much as 30% in some simple methods, 4 to 8% by visual colorimetry, and 1 to 2% by photocolorimetric procedures.

The hemoglobin is reported in grams by some laboratories and in per cent by others; the former is definitely the reading of choice since only when recorded in grams per 100 ml. of blood does the value have meaning. If it is reported in per cent, one must indicate the method used and the normal for that method. This would lessen confusion which exists at the moment.

Hemoglobin values will vary with the age and sex of the patient. The clinician should interpret a hemoglobin report and evaluate it in the light of the above stated facts, and of course, should correlate it with the clinical picture. The level at which anemia is said to occur is arbitrarily set at 12.0 grams per 100 ml. of blood.

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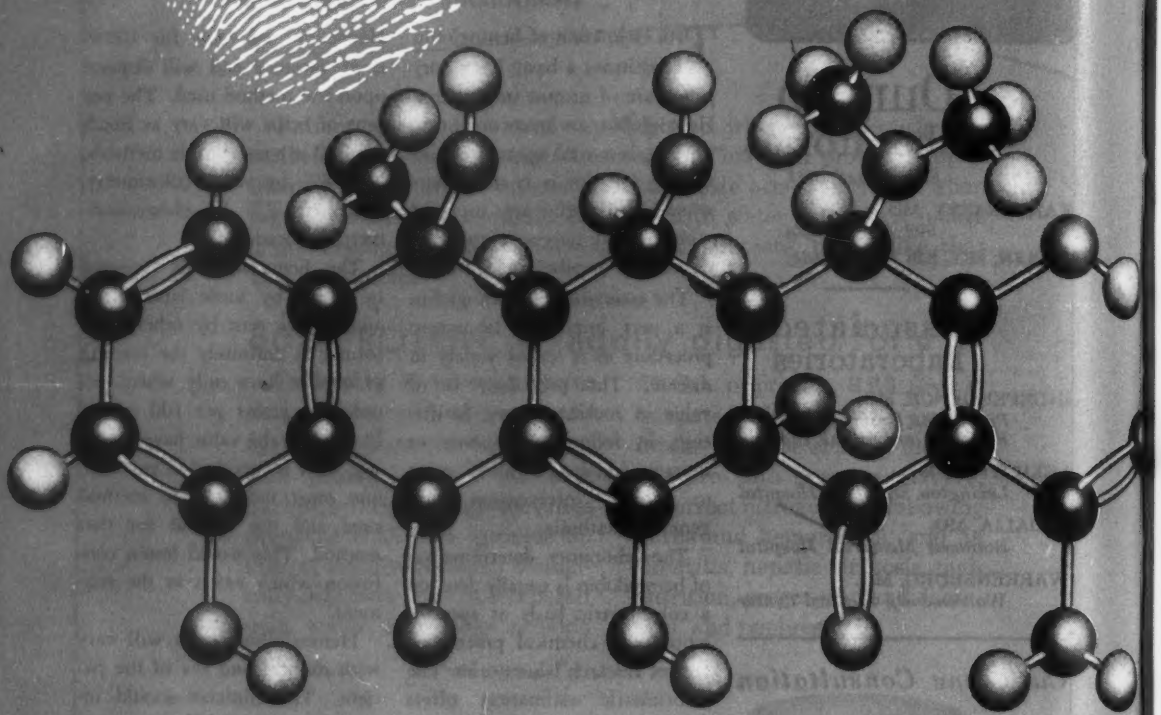

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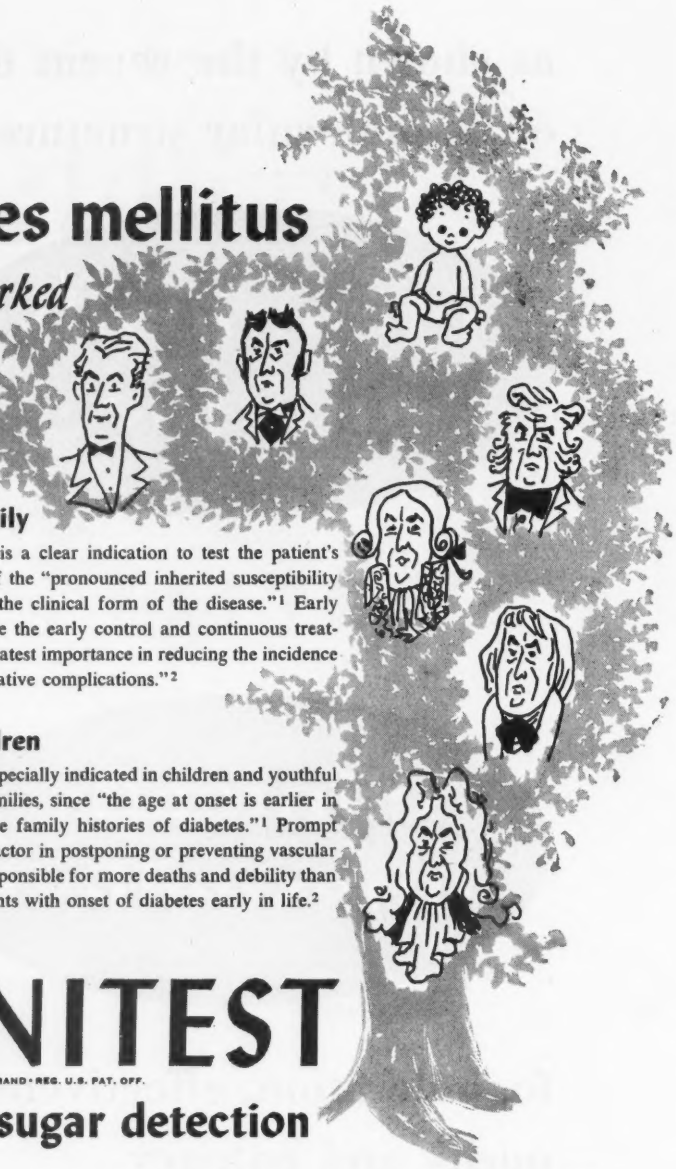

the diabetic family

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1. Watson, E. M., and Thompson, M. W.: Am. J. Digest. Dis. *18*:326, 1951.
2. Wilson, J. L.; Root, H. F., and Marble, A.: J.A.M.A. *147*:1526 (Dec. 15) 1951.

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1. Van Alyea, O. E., and Donnelly, Allen: *Arch. Otolaryng.*, 49:234, Feb., 1949.

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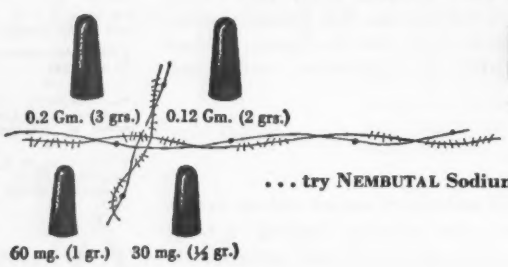

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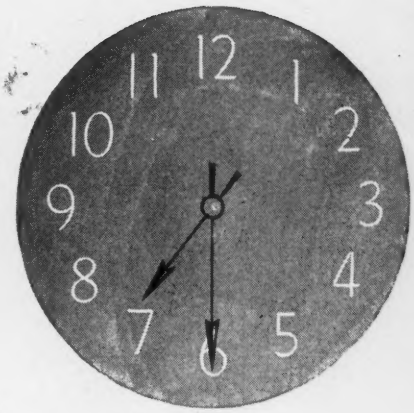

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Ward, E., Slocumb, C. H., Polley, H. F., Lowman, E. W., and Hench, P. S.,
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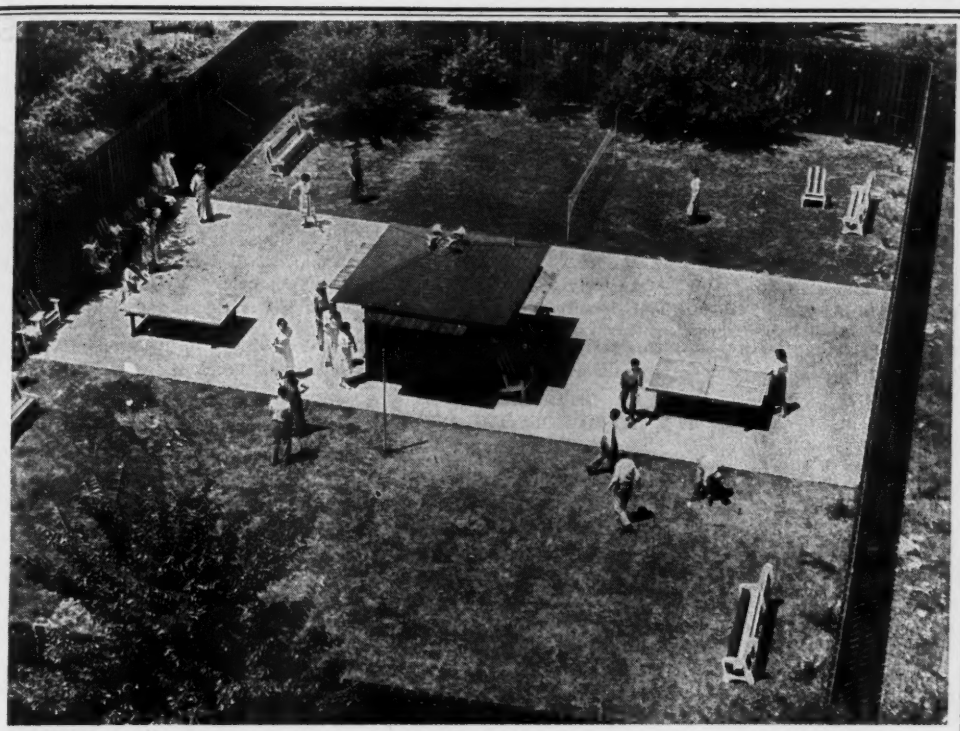

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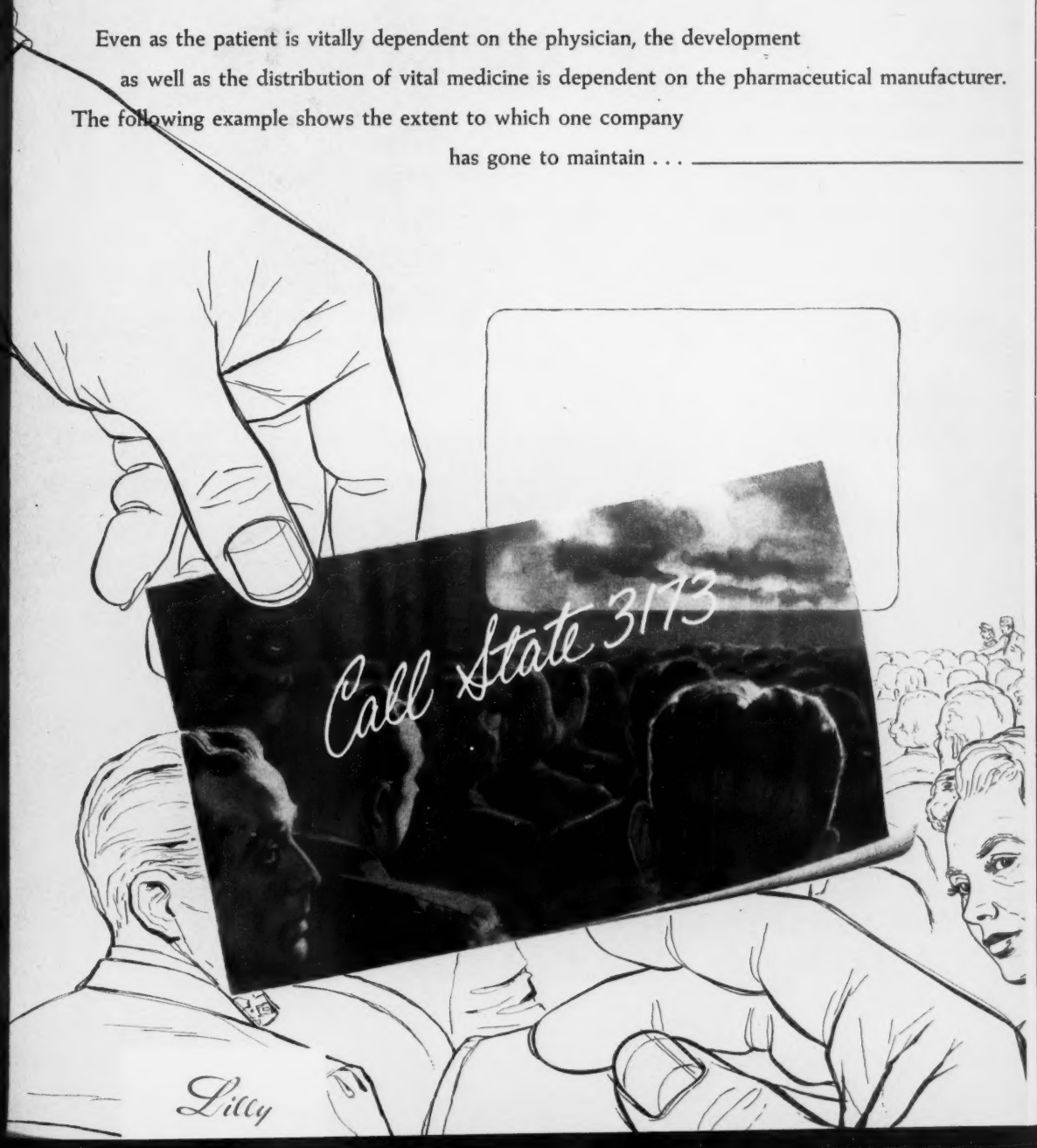

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The Possibilities and Limitations of Isotope Therapy of Cancer*

Gould A. Andrews, M.D.

Oak Ridge, Tennessee

About 13 years ago cyclotron produced isotopes were first tried as therapeutic agents. Most of the early work was with radioactive phosphorus, and this isotope was found to have distinct but not dramatic value. Small quantities of radioactive I^{130} were also utilized, and the localization of this material in thyroid cancer opened up the intriguing possibility that malignant cells might be induced to commit suicide by assimilating destructive radioactive atoms.

Almost six years ago the United States Atomic Energy Commission made available large numbers of isotopes, most of which were produced in the nuclear reactor at Oak Ridge. The public had recently seen the achievements of modern physics displayed in the most spectacular way by the atomic bomb, and when it was suggested that related new techniques might be applied against cancer, it is not surprising that the rapid conquest of this disease was expected.

The developments of subsequent years have been bitterly disappointing to those who expected sweeping advances, but not so disappointing to those who realized from the outset the limitations of isotope therapy and the slowness of any progress against cancer. Few, if any, patients have been cured by radioisotopes. However, palliative benefit has been afforded to a considerable group. Further benefit seems possible with better understanding and utilization of isotopes. Yet none of us expect that they will ever play a major role in cancer treatment.

While the therapeutic use of radioisotopes has been progressing at a snail's pace, their use as tracers in basic biologic studies has been yielding new knowledge at an almost unbelievably rapid rate. What the future value of isotopes may be to the practicing physician is anybody's guess, but it seems safe to predict that in every basic research laboratory they will be an essential tool.

Criteria for Usefulness

Several factors must be considered in relation to the usefulness of any isotope for internal therapeutic administration. These criteria would not apply for isotopes used in interstitial applicators nor for those used outside the body in teletherapy units.

The half-life should be moderately short. Although no arbitrary limits can be stated, it seems likely that there will be little therapeutic use for isotopes with half-lives less than 15 hours or more than 30 days. The rapidly decaying elements have the disadvantage that they present a relatively greater radiation hazard to those handling them since large doses must be given to produce a significant effect.

Unless the isotope is rapidly localized within the body, much of its effect is dissipated in the blood stream or near the site of administration. For example, a very short half-lived isotope given by mouth would cause a profound radiation effect upon the stomach even if it later localized specifically in some other tissue. On the other hand, isotopes with excessively long half-lives may be too slow in producing an effect and may fail to stay in the desired site during their whole period of radioactivity. They also are believed undesirable because of the increased possibility of late carcinogenic effects.

The type of radiation emitted by the isotope is of importance. Those which produce mainly high energy gamma rays tend to have the effect of total body radiation even if localized in a specific tissue. Theoretically, the ideal isotope would be a low energy beta emitter with perfect and uniform distribution limited to the tumor tissue.

The material should be non-toxic in stable form and the isotope preparation available should have a relatively high number of radioactive atoms without an excessive number of non-radioactive atoms.

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The isotope should localize or be susceptible to localization in the desired tissue with a high degree of specificity. As will be brought out later, this is the crux of the whole problem.

Problems of Radiation Treatment

Since internally administered isotope treatment is a form of radiation therapy, it is important to give consideration to the knowledge available from many years experience with other forms of radiotherapy. We must take cognizance of the sensitivity of the various cell types to radiation, although theoretically an ideal isotope localized in an ideal manner might be effective even against the most radio resistant lesion. Since the degree of localization is never perfect, and since the radiation spectrum often is such that tissues outside the tumor are radiated, the relative sensitivity of the tumor and the normal tissues is of great importance.

It is also important to recognize the non-uniformity of sensitivity of the cells in a given tumor. It is well known that a radiation dosage which may cause an almost complete disappearance of the gross tumor may leave a few malignant cells which later will become a nidus for tumor growth. Thus a true canceridical dose is difficult to obtain with isotopes as it is in conventional radiation therapy.

Again, we must be aware of the damage produced by radiation given to the normal tissues. The region around the tumor may be subjected to excessive dosage even if the isotope is well localized, depending upon its radiation characteristics. Thus the problem is the same as in conventional radiation therapy. If too much damage is done to normal tissues, excessive fibrosis and vascular occlusion may be produced. We must also consider, even more seriously than with the older forms of radiation, the problem of effect upon distant tissues, since most of the isotopes are poorly localized. In almost every instance, the bone marrow seems to be the critical tissue and the degree of hematologic damage is often an index of safety in isotope therapy.

Outline of Methods of Using Isotopes in Cancer Therapy

It may be worth while for the sake of simplicity to classify the principal ways in which isotopes are utilized.

METABOLIC LOCALIZATION. Radioiodine stands alone as the isotope which seeks out a certain type of tissue with a high degree of selectivity. The success of this localization could have been predicted on the basis of knowledge of the metabolism of stable iodine. It is obvious that there is no other element in the body which has such a characteristic localization in its metabolic pattern. It is misleading then, to say that radioiodine is a typical example, and that there are likely to be many other isotopes of similar usefulness simply waiting to be discovered. It is apparent that any other such specific deposition, if obtainable at all, will depend upon more elaborate synthetic compounds or upon some type of physiological manipulation.

Other elements have been tried, however, and there has been some slight evidence that worthwhile localization may be obtained. We have been particularly interested in gallium^{72}, an isotope which deposits in bone, particularly at the sites of growth. This isotope shows rather high specific localization in some tumors, especially in osteoblastic zones. It also tends to be deposited at the periphery of osteolytic lesions, but to a less pronounced degree. Its deposition in soft tissue tumors has been extremely variable. Up to the present, it has been of little, if any, therapeutic value, handicapped as it is by a half-life which is short in relation to the time required for specific deposition, a radiation spectrum which includes an excess of high energy gamma, and finally, most discouraging of all, an insufficient and non-uniform selective deposition in malignant tissue. At the present time, we are undertaking studies on another gallium isotope which may be somewhat more suitable. Other efforts are being made to obtain metabolic localization, and many elements and compounds have been studied for this purpose.

TOTAL BODY RADIATION. Certain diseases, particularly polycythemia vera and chronic myelocytic leukemia, respond quite well to radiation of the total body. These diseases can also be treated quite effectively with radioactive phosphorus. Although the phosphorus shows some specific localization in marrow, liver, lymph nodes, and spleen, it is widely distributed, and the difference in concentration between various tissues is not striking. Therefore, since its effects are quite similar to those obtained with total body radiation, it seems erroneous to emphasize the relatively slight tissue specific concentration which it has. This isotope has proved to be a highly convenient form of treatment for polycythemia vera and seems to have value in certain selected cases of leukemia and lymphoma. In general, it has yielded little benefit that could not have been obtained by other means.

The possibilities that it may produce a higher instance of acute leukemia in polycythemia vera and a higher incidence of acute blast cell crises in myelocytic leukemia, however, are cause for considerable discussion at the present time. Radioactive sodium, while not convenient to use, has been shown to produce benefit in the same diseases which are helped by total body radiation and this produces an even more uniformly diffused radiation than that resulting from radioactive phosphorus.

MECHANICAL LOCALIZATION. With the realization that there are profound limitations on metabolic methods of localization, there has been

an effort to utilize more artificial means of achieving localization in malignant tumors.

The direct injection of tumors with colloidal radiogold has been developed particularly by Dr. Paul Hahn. The advantage of this method is that it is theoretically possible to achieve very high radiation dosages within the tumor without producing much damage to surrounding tissues. The disadvantages of the treatment are that it is impossible to produce a unform distribution of the colloid in the tumor and that it is often impossible to know the exact limits of the tumor and therefore to place the gold properly. There is also considerable hazard to the physician who undertakes to make the injection. At present, this form of treatment seems to have very limited value and is only palliative at best.

Recently there has been considerable interest in the direct injection of tumors of the prostate gland. It may be that this organ is particularly suitable for such treatment, and preliminary results are reported to be encouraging. The fact that the radiogold, in some cases, is picked up by lymphatics and carried to adjoining lymph nodes may add to the possible value of the treatment. This lymphatic distribution has been utilized in the treatment of carcinoma of the cervix. The radiogold is injected into the parametrial areas and is believed to give an effective local radiation and to travel a considerable distance to lymph nodes draining the area. In this disease it is not used as a definitive treatment but as a part of a complete treatment program. It is too early to evaluate these new forms of gold injection treatment.

This isotope, gold^{198}, in colloidal form, has also been used by intravenous injection. When given by this route, it is taken out of the blood stream by the reticuloendothelial tissues of liver, spleen and bone marrow, and therefore does give radiation to a certain type of tissue. Possibly this could be considered a form of metabolic localization. It has proved of value in treatment of chronic myelocytic leukemia and to a less extent in chronic lymphocytic leukemia. In the latter disease, its disadvantage is that it usually gives inadequate therapy to lymph nodes. We have been interested in giving this isotope to patients who have metastatic carcinoma in the liver, since a very large proportion of the isotope is segregated in this organ. Our experience has been quite disappointing; in every instance the metastatic nodules have been too large to receive much effect from the beta radiation in the adjoining normal liver tissues, and there has been essentially no deposition at all of the gold within the metastatic nodules.

The same isotope, colloidal gold^{198}, has been used for injection into body cavities. We have had considerable experience in the treatment of patients with ascites or pleural effusion caused by malignant neoplasms involving the surfaces of these cavities. By injecting the radiogold directly into the cavity, it is often possible to control the effusion although the fundamental course of the neoplasm is apparently not greatly altered. It appears likely that this treatment or a similar treatment with some other isotope may replace x-ray therapy in the treatment of patients in whom the only aim is to control effusion. Attempts to treat lesions in other body cavities, such as the urinary bladder and paranasal sinuses, have been made, and there is some promise that isotopes will offer value in treating lesions in these areas. These studies are preliminary at the present time.

Radium is, of course, a naturally occurring isotope, and it has been used for many years in various types of intracavitary and interstitial applicators. More recently cobalt^{60} has been found to be of value when used in a similar manner. The cobalt has the advantage of being relatively inexpensive and of being more flexible and adaptable since it can be produced in many different types of applicators. It also has the advantage of more uniform type of radiation.

Radioactive phosphorus has been used by means of external application for the treatment of superficial malignant tumors. This isotope can be deposited on an individually constructed applicator which will fit the exact dimensions of the tumor, and by this method it is possible to obtain an intense but relatively non-penetrating radiation limited to the area covered by the applicator.

TELETHERAPY UNITS. Radioisotopes can be used in special shielded units which make it possible to direct the radiation into the body from an external source which is at a considerable distance from the skin. These units produce an effect similar to x-ray therapy. They are outgrowths of similar instruments devised for the use of radium. The artificially produced isotopes which are now available, however, seem much superior to radium for this purpose. The isotopes which may be suitable for this use are cobalt, cesium, europium, tantalum, and iridium. Of these, cobalt has had a good deal of study and cesium is now the subject of preliminary investigations.

The advantages of teletherapy units are multiple. The initial cost is low in comparison to the cost of comparable x-ray therapy units. However, the radioactive sources themselves, since they are the result of government supported research, are difficult to appraise in terms of what they would cost if privately produced. A second advantage is that the

maintenance of such a unit will presumably be a great deal simpler and cheaper than the maintenance of comparable x-ray therapy unit. Furthermore, the teletherapy instruments will be more flexible than comparable super-voltage x-ray. There are some differences in the quality of radiation, cobalt^{60} being free of the relatively non-penetrating radiation which is part of the spectrum produced by x-ray. Whether this difference in type of radiation will be of significant value clinically is yet to be determined. It appears that these teletherapy units will not revolutionize the accomplishments in treatment of carcinoma, but that they will bring a form of radiation comparable to supervoltage therapy into a price range which will greatly increase the availability of this treatment.

Summary

Radioisotopes, while failing to offer any ultimate solution to the cancer problem, are contributing significantly to cancer therapy. To be used effectively they must be properly integrated with existing forms of treatment. They serve to emphasize that the treatment of cancer is not simple or stereotyped and that for each individual case there should be a carefully planned program using whatever modalities seem most suitable.

Skin Injury by Fluorescent Bulb*

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The danger of skin cuts by fluorescent bulbs is known from several reports,[1,2] and wide excision of the wound, when first seen, is recommended as the only effective prevention of chronic ulcers. The following case is reported because a laceration by fragments of a fluorescent bulb did not heal for two years. Wide excision of the draining lesion and of the healthy appearing surrounding tissue, with transplantation of a full skin flap, was necessary after two years of suffering.

Case Report

Miss L. B., age 24, entered the Hertzler Clinic on February 21, 1951, with the complaint of a recurrent draining ulcer on the right arm. In February, 1949, while changing a fluorescent tube in her desk lamp, she accidentally bumped the tube. It exploded and cut her on the flexor surface of her right lower arm. She paid no attention to the injury. However, four days later she found a small piece of glass in the wound. In a hospital, a superficial debridement of the wound was performed and the wound edges were approximated with adhesive tape.

During the following five weeks the wound drained intermittently, and the patient found seven or eight pieces of glass in all, in the wound and adherent to the dressings. The skin became painful, hard, and almost purple in color, and several draining sinus tracts had formed. Local dressings with various ointments were without effect. Therefore, in June, 1950, the inflamed area with the sinus tracts was resected and the defect closed with sutures. Two weeks after the operation, draining sinuses again became apparent; they closed for a few weeks only to break open again. A plaster of paris cast was applied to the right arm, to make any mechanical injuries to the lesion impossible. The wound became closed. However, in the fall of 1950, draining sinuses appeared once more.

On February 22, 1951, a radical excision of the lesion was performed. The defect was covered with a full thickness skin flap from the anterior abdominal wall. The postoperative course was uneventful, the transplant healed well, and there has been no recurrence of the draining lesions during the past year. At present the patient has full use of her right arm.

Pathologic Description of the Surgical Specimen

(C. A. Hellwig, M.D.)

Gross Pathology: The surgical specimen was an elliptical piece of skin, measuring 8 x 4.5 cm. The attached fat tissue was 16 mm. thick. On the surface was a healed scar, four cm. long, running oblique to the long axis of the specimen. There were two draining sinuses near the center of the scar; one had a diameter of two mm., the other of 1.5 mm. Both were surrounded with hard, retracted scar tissue. There were also three sinus openings near the margin, which measured between three and four mm. and were covered with a thin bluish layer of epidermis. On the lower surface, corresponding to these tracts, were hard, whitish, granular areas. On cross section most of the tissue consisted of fat. Surrounding the tracts the tissue was hard, whitish, and translucent. Section through the scar revealed a hard, yellow, necrotic appearing mass with irregular outline, measuring 2 x 3 mm. in diameter.

Microscopic Findings: The epidermis covering the surface was thick and appeared normal. In the corium and subcutaneous tissue many single and conglomerate tubercles were noticed. They con-

*Presented before the Harvey County Medical Society, September, 1951.

Figure 1. Microscopic section of skin lesion two years after injury. Active beryllium tubercles without caseation. Magn. x 120.

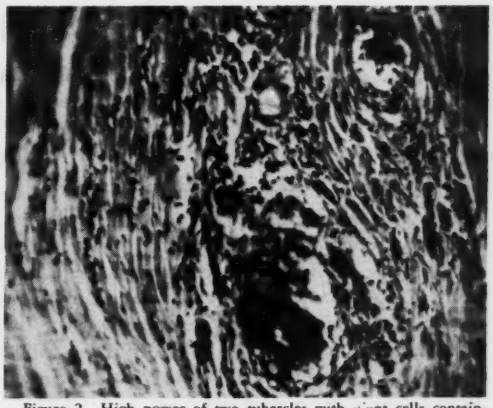

Figure 2. High power of two tubercles with giant cells containing conchoidal bodies. Magn. x 240.

sisted of epithelioid cells, lymphocytes and multinucleated giant cells of the Langhans' type. Some of the latter had dark stained inclusions which were not anisotropic in polarized light. No caseation was found in any of the tubercles. The surrounding fibrous tissue was diffusely infiltrated with histiocytes, lymphocytes, and fibroblasts.

The histological diagnosis was beryllium granuloma of the skin.

Spectographic Analysis: Formalin-fixed tissue was submitted to F. R. Dutra, M.D., of the Kettering Institute, Cincinnati, Ohio. His report follows: Microscopically the lesion certainly is typical for beryllium granuloma of the skin. Spectrographic analysis revealed 0.58 micrograms of beryllium per 100 gr. of tissue.

Discussion

The most interesting microscopic findings in our case were the active granulomatous lesions still present two years after the injury, in spite of two attempts to excise the wound. This can be explained only by the activity of macrophages which carry beryllium particles from the original lesion into the surrounding tissue, beryllium being insoluble in tissue fluid. There were characteristic inclusion bodies within the giant cells. The shape varied from a rounded body to a distorted, stretched-out, elongated one. These bodies stained black with hematoxylin and eosin.

Summary

A case of cutaneous granuloma injury following laceration by fluorescent light bulb which existed for two years is described. The lesion was accompanied with intermittent draining sinuses until wide excision of the involved area with skin transplantation effected a permanent cure. Histological and spectrographic findings were typical for beryllium granuloma.

The tenacious chronicity of beryllium granuloma is due to the fact that the implanted beryllium is carried by macrophages widely into the surrounding healthy tissue and produces draining sinuses which defy any conservative treatment. Active tubercle-like granulomas were still found two years after injury.

Skin lacerations by broken fluorescent bulbs require excision of the wound with a wide margin of apparently healthy skin.

Prevention of the cutaneous lesions can be accomplished only if all contaminated tissue is removed, preceding initial wound closure.

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The Complications and Diagnosis of Infectious Mononucleosis

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An attack of infectious mononucleosis in its so-called usual and ordinary form is considered benign and more or less self-limited. This concept may be true. However, in recent years there have been amassed many reviews and case reports attesting to the extremely varied manifestations of this disease, acute and chronic, mild to fatal, which should make us view each "ordinary" case of infectious mononucleosis with suspicion and concern.

The history and many recent large-series reviews of this disease, with their emphasis on the multiplicity of signs and symptoms, make for interesting reading. However, it is not the purpose of this paper to enter into a discussion of these features, but rather to again point out certain specific aspects that may make differential diagnosis more difficult and certain complications of possibly more serious consequences.

Because of the few fatalities in infectious mononucleosis the pathology has not been too well delineated. However, Custer and Smith[1] in their review of nine autopsies were able to make a definite clinico-pathological correlation in all their cases and to observe that "there are as many lesions of infectious mononucleosis as there are organs of the body, although the degree of involvement varies from case to case." In general, "the histologic changes revealed more or less generalized lesions resembling those of certain known virus diseases, notably perivascular aggregates of normal and abnormal lymphocytes." Despite the scantiness of the pathological literature, certainly this fine review begins to give us some clue as to the background of the many variations of this disease.

Blood

Extreme variations in the white blood count and differential may occur in the course of infectious mononucleosis. However, at some stage of the disease process a characteristic picture usually occurs which involves an increase in the mononuclear cells. These are of three types:[2] (1) small lymphocytes; (2) monocytes, both of these appear normally in the blood; and (3) large mononuclear leukocytes which are not normally observed in the blood. The "mononucleosis" is due mainly to the presence of these abnormal cells. These latter cells may have been divided into three types, according to the classification of Downey and McKinley.[3] However, their general description is as follows:[4] "They are variable in size, shape and staining. The nucleus, whatever its shape, is usually stained darkly and coarsely. The cytoplasm may be pale blue but is more often deeply basophilic and vacuolated, presenting a foamy appearance."

Most large series reports agree that at onset, in a high percentage of cases, there is a moderate leukocytosis. In mild cases there may be no change in the myeloid series, but in severe forms the white blood count may reach leukemoid levels with a high per cent of polymorphonuclear cells in the differential. In a resume of 556 cases seen by Wechsler et al[5] four per cent of the cases attained a count of 30,000 or over. This initial polynucleosis may be a possible source for diagnostic error since infectious mononucleosis is usually though of in relation to lymphocytosis. In addition, since the incidence of splenomegaly in published reports is about 50 per cent, the diagnosis of leukemia may be entertained. Although many of the leukocytes seen in infectious mononucleosis appear abnormal, very few of them contain nucleoli; also, the atypical lymphocytes do not show granules when stained by the peroxidase method. Thus they can be distinguished from cells of the granulocytic series and, to some extent from the monocytes.[2]

In 1950 Raftery and Thompson[6] made an extensive review of the literature and failed to find any report of the association of infectious mononucleosis with malignancy of the reticulo-endothelial system. They reported a case of infectious mononucleosis in a 21-year-old white female, followed in six weeks by subacute granulocytic leukemia. When first seen, this case showed the usual abnormal lymphocytes, typical of infectious mononucleosis, with a heterophile agglutination test of 1:448. A differential test by the Davidsohn technique was not reported.

In a recent excellent review of infectious mononucleosis by Tidy,[7] he states: "The blood changes should not cause difficulty in differentiation from leukemia when the patient is seen in the acute stage. In acute leukemia, the toxic symptoms are always severe. An occasional, but extremely difficult diagnosis, may be caused by the rare slowly progressive chronic lymphoid leukemia. In the earlier stages, there are periods of exacerbation with pyrexia and moderate glandular swelling. The lymphocytes for several years may be only at the upper limits of normal. They gradually creep up and

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the diagnosis, long suspected, slowly becomes confirmed. The diagnosis is difficult when it is asked for on a patient some months after a pyrexial attack with lymphocytosis considered to be infectious mononucleosis. Either lymphocytosis or glandular swelling may persist for several months after infectious mononucleosis, but if both features are present for six months the diagnosis must be considered in doubt, unless it has been fully established. I have watched three such cases, originally diagnosed doubtfully as infectious mononucleosis, gradually develop fatal lymphoid leukemia over three to ten years."

Shortly following the onset of illness there is usually a reduction in the absolute neutrophil count, and since these patients are not often seen before the fourth or fifth day of illness, a leukopenia or granulocytopenia with an associated increase of the mononuclear cells, as described above, may be the presenting blood picture. In Milne's[4] experience with 141 cases the average per cent of polys on admission was 39, later falling to 20-25 per cent. He reports one case of four per cent neutrophil count. In such unusual cases of extreme granulocytopenia, the diagnosis of agranulocytosis may be suggested. The mononuclear cells may not reach their peak until the second or third week, and the abnormal "leukocytoid" lymphocytes may average from 10 to above 50 per cent.[5]

In regard to bone marrow studies the prevailing opinion is as described by Wintrobe:[2] "The sternal puncture is chiefly of value from a negative standpoint in the sense that findings characteristic of leukemia are absent." With this in mind Hovde and Sundberg[8] recently made bone marrow studies in 23 cases of infectious mononucleosis, eight cases of brucellosis, two of sarcoidosis, two of tuberculosis, 15 of chronic lymphatic leukemia, and 19 of acute and subacute lymphatic leukemia. Their findings are interesting in that they describe two changes in the bone marrow of infectious mononucleosis patients which they consider of value in differential diagnosis: lymphocytosis with the typical "leukocytoid" lymphocytes of infectious mononucleosis in 70 per cent of cases and granulomatous lesions in 48 per cent of cases. The degree of lymphocytosis was shown to be less than that of lymphatic leukemia and was not found in brucellosis, sarcoidosis, or tuberculosis. The granulomatous lesions, when present, were not always easily distinguishable from those of brucellosi, sarcoidosis, and tuberculosis.

Anemia, thrombocytopenia, purpura and hemorrhagic manifestations have been considered as rare complications of this disease. Indeed, as early as 1922, Longscope[9] declared that bleeding and purpura did not occur in infectious mononucleosis and could be used as differential diagnosis from leukemia. The infrequency of anemia is epitomized by the reports of Read and Helwig[10] and Wechsler et al.[5] The former authors reported only six cases of anemia in 300 cases and the latter group found no anemia in a study of 556 cases.

However, Bernstein in his excellent monograph in 1940,[11] stated that the presence or absence of bleeding cannot be used as a differential point from leukemia. Since then numerous reports have been made of infectious mononucleosis complicated by acute hemolytic anemia and/or thrombocytopenic purpura, associated in general with complete recovery on subsidence of the infection.[10,12,13,14,15,16,17,18,19,20,21,22]

A perusal of these reports reveals thrombocytopenia ranging from less than 10,000 to 100,000. In addition, there were included hemorrhagic manifestations such as petechiae or ecchymoses involving conjunctiva, tongue, gums, buccal mucosa, and skin. Nosebleeds, hemoptysis, hematemesis, tarry stools, hematuris, and menorrhagia are also reported. Bleeding times were generally increased and coagulation time normal. The hemoglobin has been reported as low as 5.5 gms. One such case study[19] reported a positive Coombs test. Two of these reports, that of Dameshek and Grossi[12] in 1946 and that of Wilson et al[21] in 1949, involved cases of continued bleeding and anemia so severe that splenectomy was performed. In each case operation was successful and recovery complete. Dameshek and Grossi suggested that "in the presence of well defined splenomegaly in infectious mononucleosis a state of hypersplenism might conceivably result with the production of megakaryocyte inhibition and thus thrombocytopenia." This explanation and concept seems to apply well to many of these cases. However, Read and Helwig[10] hypothesize a possible depression of bone marrow activity from an infectious granulomatous process.

Spleen

In regard to splenic enlargement, Stevens, Bayrd and Heck[23] in studying 210 sporadic cases of infectious mononucleosis found that in 67 per cent of those cases in which it was present the enlargement was encountered from the 10th to 21st days of the illness. Enlargement was still present four months after the acute stage of the disease had subsided in two cases and in one case still palpable at eight months.

Of the 15 reported deaths in infectious mononucleosis, eight have been due to rupture of the spleen.[24] From a review of their autopsy material, Custer and Smith[25] interpreted this complication as resulting from a rapid splenic enlargement, stretching of the capsule and thinning of trabeculae. The exciting cause is often trivial, as exemplified by possibly the first reported case in 1941.[26] This was

apparently a spontaneous rupture in a 23-year-old white male, who was operated with recovery.

On the basis of their studies, Custer and Smith made these three additional points, all possibly of some clinical import: (1) palpation of the spleen in suspected cases should be omitted; (2) splenic rupture is unlikely to occur during the first two weeks of the disease; (3) rupture of the spleen is followed by reversal of the differential formula of the leukocytes with the neutrophils predominating, and this may prove confusing.

Jaundice and Hepatitis

Jaundice was first recognized as a complication of infectious mononucleosis by Mackey and Wakefield[27] in 1926. In 1944 three reports estimated that from 21 to 35 cases of jaundice in infectious mononucleosis had been reported. Since that time the total has risen to approximately 100 cases[28] and the incidence of jaundice in different series has ranged from zero to 13 per cent. In Wechsler's[5] series of 556 cases there were 34 cases, or six per cent, varying in duration from 11 days to 48 days, with the highest icteric index recorded at 100.

As late as 1942 jaundice was interpreted as evidence of common bile duct blockage by enlarged nodes. However, in that year Kilham and Steigman[29] demonstrated focal acute hepatitis by punch biopsy in a deeply icteric patient and suggested that hepatocellular damage might be the cause of clinical jaundice in infectious mononucleosis. This concept is now well established on the basis of autopsy, biopsy, chemical and clinical observations.

In a pilot study of considerable import, by Cohn and Lidman[30] in 1946, it was shown that hepatic dysfunction occurs even in non-jaundiced patients. The impetus for this investigation was the increasing evidence of similar symptomatology between infectious mononucleosis and infectious hepatitis. Fifteen successive cases of infectious mononucleosis were studied and although the serum bilirubin was normal, every case demonstrated impairment of liver function by more than one test. All cases exhibited bilirubinuria, thymol turbidity values ranged from 5.1 to 14.3, B.S.P. retention varied from 11 to 43 per cent, electrophoretic analysis of sera showed a slight decrease in concentration of serum albumin and greater than normal figures for alpha and beta globulins and a rather marked increase in gamma globulin. All these findings are comparable with infectious hepatitis.

Confirmatory reports soon followed. In 1947, DeMarsh and Alt[31] studied 19 cases without jaundice using B.S.P., cephalin flocculation, and icteric index. Some degree of hepatic damage was present in all cases. Liver tenderness was present in seven per cent of their cases, usually transient, but persistent for four weeks in one case. Apparently, there was some rough correlation between the severity of symptoms and the degree of hepatitis, but no correlation to the height of the heterophile antibody titer.

A. S. Evans also reported 19 cases without jaundice, in 1948.[32] The cephalin flocculation test was found to be abnormal (two plus or more in 24 hours) in 95 per cent, and in two instances was abnormal before the heterophile antibody titer had reached a significant level. The thymol turbidity test was elevated in 68 per cent, ranging from 4 to 10 units. This change usually appeared later and was more transient than in the cephalin flocculation. The alkaline phosphatase showed values from 4 to 11.5 Bodansky units in 43 per cent. In this particular report a control study was made using upper respiratory infection cases in which infectious mononucleosis was ruled out, but severe enough the patients had to be hospitalized. The following results were obtained: cephalin flocculation negative in 22; thymol turbidity, one positive in 13. It was concluded that the flocculation tests were of value in differentiation of hepatitis without jaundice from uncomplicated U.R.I.

Jordan and Albright[33] made similar observations on 24 patients with infectious mononucleosis, two of whom were jaundiced. In their series the maximum number of changes in hepatic function tests was observed during the second and third weeks of the disease, and flocculation disturbances persisted more than two months in a fourth of the patients.

Electrophoretic studies of serum proteins in seven cases of infectious mononucleosis by Sterling[34] in 1949 have confirmed Cohn and Lidman's original observations in this regard.

The largest series of cases studied so far, from the standpoint of liver function, is that of Bennet et al.[35] One or more abnormal tests were found in 83 of 90 patients. They suggest that the B.S.P., cephalin flocculation, thymol turbidity, and quantitative Van den Bergh are best for screening purposes. The cholesterol and cholesterol esters were found abnormal in only two of 13 (16 per cent) patients. In a follow-up study, seven of these patients were found to have evidence of chronicity or recurrence. One was still symptomatic at the end of two years, a second was symptomatic but still had 11 per cent B.S.P. retention at the end of two years, and a third was mildly symptomatic with abnormal reactions at 31 months. Four other patients showed abnormal reactions at seven to nine months.

In the presence of hepatic dysfunction, both with and without jaundice, the necessity for differentiation from infectious hepatitis becomes obvious and

is stressed in most of these reports. Both infectious mononucleosis and infectious hepatitis may present symptoms of anorexia, nausea, asthenia, lassitude, easy fatiguability, and diminished exercise tolerance.[30] Infectious hepatitis may present adenopathy, splenomegaly (10 to 15 per cent of cases) and leukopenia with a relative lymphocytosis and atypical lymphocytes in the blood. Hepatomegaly is usually reported in 10 to 15 per cent of cases of infectious mononucleosis. This overlap of similarities extends to the pathological findings as well. Custer and Smith[1] state that "the liver lesion is essentially a periportal hepatitis. It is hardly distinguishable from liver changes in the milder cases of epidemic hepatitis as observed at biopsy."

The discrepancy betwen signs and symptoms and the results of the hepatic function test is epitomized in the report of Kass and Robbins,[24] concerning a case of infectious mononucleosis with minimal clinical manifestations and death by rupture of the spleen. At autopsy, aside from the splenic pathology, a severe hepatitis was encountered.

Granted that the adenopathy, splenomegaly, and blood picture are more distinctive in infectious mononucleosis, nevertheless it is conceivable that the differentiation in a particular case might rest mainly on the results of the heterophile antibody test, and since in the occasional case this test is negative, occasional cases of these two diseases may be indistinguishable.

Such a situation is exemplified by the case report of H. L. Abrams.[28] This case involved a 30-year-old male, visibly icteric for 11 weeks, with splenomegaly, hepatomegaly, liver function tests indicating hepatitis (including a peak serum bilirubin of 27.5 mgm. per cent), no significant adenopathy, leukopenia with relative lymphocytosis. The heterophile antibody test became positive (1:896) only after eight and a half weeks of illness. Abrams summarized as follows: "This case resembled a severe case of infectious hepatitis in all respects except the peripheral smear. The negative Paul-Bunnell tests during the first eight weeks of the illness might well have been accepted as evidence that this was, indeed, a case of infectious hepatitis, especially in view of the frequent occurrence of lymphocytosis and atypical lymphocytes in infectious hepatitis."

In view of this case and the above data, perhaps many cases heretofore labelled as infectious hepatitis may have actually been infectious mononucleosis.

On the basis of these many reports indicating a high incidence of hepatic dysfunction in cases of infectious mononucleosis, both with and without jaundice, many authors are now urging that all cases be treated as though they have an associated infectious hepatitis. If this therapeutic concept is followed, the differentiation of the two diseases may seem academic. However, since to date there is no data with which to evaluate the late complications of the hepatitis of infectious mononucleosis and since the long-term prognosis of the two diseases, infectious mononucleosis and infectious hepatitis, may be entirely dissimilar, the importance of repeated heterophile antibody tests in questionable cases is emphasized.

Isaacs,[36] from a study of 206 cases of infectious mononucleosis, found 53 cases with persistent asthenic symptoms and atypical cells in the blood stream from three months to several years and coined the term "chronic infectious mononucleosis." Unfortunately, no liver function studies were reported from this group of cases.

Kass and Robbins[24] in their pathological review state, "The conclusion seems warranted that despite the intensity of the anatomic and clinical changes the hepatic lesion in infectious mononucleosis is more benign than its counterpart in infectious hepatitis. One reason for such relative benignity may be that there is little tendency toward necrosis in the liver in infectious mononucleosis and therefore less likelihood of scar formation."

However, recently, Leibowitz and Brody[37] have reported a case which they believe the first documented instance of cirrhosis of the liver following infectious mononucleosis. The diagnosis of cirrhosis was by biopsy; the diagnosis of infectious mononucleosis was based on serological tests, a rising heterophile antibody titer to 1:800 on the 60th day of illness with a subsequent fall to normal. A Davidsohn "differential test" was not done. This patient was first seen one month after onset of illness, and no atypical lymphocytes were noted. They exclude infectious hepatitis on the basis that such a high heterophile antibody titer has never been seen in that disease.[38] There was a history of poor diet in this case. Considering our limited etiological knowledge in cirrhosis, this may have been a primary factor.

Lung

Involvement of the respiratory tract with both clinical and x-ray findings similar to atypical pneumonia has been described not infrequently. Wechsler et al,[5] found 14 cases out of 556 with x-ray changes of this type. Of these 14 cases the symptoms were those usually found in atypical pneumonia as manifested by the characteristic cough, the asthmatic wheezing, the disparity of physical signs and the failure to respond to sulfadiazine.

Recently two separate reports have been made of the roentgenological aspects of infectious mononucleosis.[39,40] Aside from the splenic and hepatic enlargement, which may be easily distinguished by x-ray in many cases, the main changes on chest x-ray recorded enlargement of the hilar and medias-

tinal lymph nodes, which must be distinguished from that associated with other diseases; and pulmonary parenchymal infiltration often distinguishable from atypical pneumonia.

One of these reports[39] was based on 75 patients with infectious mononucleosis. Of this group, 43 had chest x-rays and seven showed one or both of the above abnormalities. It noted that in none of the cases was pneumonitis suspected clinically; it was an incidental finding on the chest x-ray. This suggests, in the light of the experience of Wechsler and his group, that symptoms may or may not be present. The duration of findings on chest x-ray were varied from one week to three months.

That diagnostic difficulties from a roentgenological viewpoint are encountered is suggested by the case report of J.S. Herschboeck.[41] In this case the film taken the seventh day after admission indicated bilateral bronchopneumonia. Five days later the roentgenologist suggested miliary tuberculosis as the probable diagnosis. Three weeks later the lung cleared completely.

As a general rule, lymphadenopathy and splenomegaly are of markedly low incidence in atypical pneumonia.[42,43] In addition, the incidence of significant (1:128) titers of cold hemagglutinins has been reported as about 54 per cent.[44] These factors should aid in the clinical and laboratory differential diagnosis of these two diseases. However, a few cases of infectious mononucleosis with high titers for cold hemagglutinins have been reported.[45] In 1950, Evans[46] did 89 cold hemagglutination titers on 56 patients with infectious mononucleosis. The highest titer was 1:32 (10 per cent) and the great majority (84 per cent) were under 1:8. However, this author makes a plea that in those diseases in which the serum may contain cold hemagglutinins in high titer, a determination for the coexistence of a heterophile antibody should be carried out by some method not requiring exposure to cold temperatures.

Heart

Cardiac signs and symptoms are uncommon, but a few cases have been reported here and there. Wechsler et al[5] found in their series one case, a Negro, age 24, with typical infectious mononucleosis, substernal pain, bradycardia, sinus arrhythmia, P-R interval of 0.24 to 0.44 seconds, a systolic murmur and moderate cardiac enlargement. Because of this, electrocardiograms were taken on 223 patients. Of this group, 53 patients (or 23 per cent) showed abnormal tracings in some respect. Cardiac enlargement occurred in only three. There were no cardiac symptoms except an occasional complaint of sharp precordial pains.

In four cases of Graybiel and Evans,[47] the T-waves were lowered or inverted in all leads, suggesting pericardial involvement with gradual return to normal during convalescences. Logue and Hansen[48] have recorded a case of first degree heart block with prolonged P-R interval. In the autopsy cases studied by Custer and Smith,[1] pericarditis was not demonstrated. However, lesions were found in the heart muscle in six cases. Extensive residual areas of myocarditis after 30 days were found in one.

Central Nervous System

Apparently the incidence of nervous system involvement in infectious mononucleosis is quite small. In a review of 141 cases seen between 1935 and 1945, Milne[4] states that in no case was meningitis suspected, and no lumbar puncture was done. However, some of the case reports in regard to this complication are most dramatic and arresting. Recently Bernstein and Wolff[49] made an excellent review of this particular facet and found that between 1931 and 1947 only 28 reports had been submitted to the literature; these included 46 patients, 34 of whom they were willing to accept as bona fide cases of infectious mononucleosis.

The disease process may involve the brain, meninges, spinal cord, cranial and peripheral nerves, in the form of meningitis, encephalitis, meningo-encephalitis, meningo-encephalitis with acute polyneuritis, and peripheral neuropathy. Apparently the combinations and sequence of involvement may be extremely varied. Correlation with the onset or severity of the ordinary manifestations of infectious mononucleosis is not constant;[50] neurologic and glandular (or febrile) symptoms may be simultaneous or may precede one another. In those cases where symptoms of central nervous system involvement precede, the diagnosis could easily be missed unless it were thought of and considered in the differential. In addition, Tidy has stated that when the neurologic system involvement is severe, the changes in the blood picture tend to be delayed.

The spinal fluid changes recorded have consisted mainly of moderate increase in cells and/or protein. The cells are mainly lymphocytes. Spinal fluid pressure is occasionally increased; sugar and chlorides are normal; changes may persist beyond the time of clinical recovery. Abnormalities of the spinal fluid may occur without mental, motor or sensory changes.[51]

The great majority of reports emphasize the negativity of heterophile antibody titers in spinal fluid. However, Silverstein et al[52] have reported demonstration of spinal fluid heterophile antibody in the same absorption pattern as the blood, by use of certain modifications of techniques.

The overall prognosis in these cases with central nervous system complications is good. Bernstein and Wolff[49] report complete recovery in 85 per cent

of cases in periods ranging from a few days to several months.

A few of the specific clinical manifestations mentioned in the literature are worthy of reviewing. Hubler et al[53] have reported a case manifested by stupor and convulsions. One patient with encephalomyelitis had considerable muscle weakness and sensory changes and signs of cerebellar damage many months after apparent recovery from the acute process.[54]

In 1947, Ashworth and Motto[55] reported infectious mononucleosis in a 19-year-old soldier who had three plus diopter papilledema, noting this was the first case recorded without accompanying meningitis or encephalitis. J. J. Piel et al[56] presented a similar case, manifested by blurring of vision and pain on motion of the eyes, and were of the opinion that the bilateral papilledema in their patient represented a primary optic neuritis rather than increased intracranial pressure.

H. Tidy has expounded the similarities between infectious mononucleosis and benign lymphocytic meningitis.[7,50] He states that "from a study of available publications and from personal experience, I can find no points of difference between neurological symptoms of benign lymphocytic meningitis and those of glandular fever or between the changes in the central spinal fluid in these conditions . . . in published records of cases of benign lymphocytic meningitis (search not exhaustive) I failed to find a single case in which glandular fever or infectious mononucleosis is even mentioned, much less excluded." He submits that unless this differential diagnosis is made, future cases of benign lymphocytic meningitis cannot be accepted as an entity.

In a few instances there has been striking albumino-cytologic dissociation. In the two cases with which Ricker et al[57] were directly concerned, flaccid paralysis with absent deep tendon reflexes was noted. One of their patients suffered from numbness of the extremities. Death was from respiratory paralysis. The authors expressed the belief that their cases represented an association of infectious mononucleosis and the Guillain-Barre syndrome and presented histologic evidence as support.

N. E. Creaturo[58] reported a case of infectious mononucleosis simulating the Guillain-Barre syndrome, with recovery. This case developed fairly rapidly ascending type paralysis with facial diplegia and paralysis of the right side of the palate and distinct nasal twang, pain in both legs and tingling sensation in hands and feet. The spinal fluid total proteins were 168 and cells negative. Other similar reports are in the literature.[59,60]

Cases of isolated peripheral nerve involvement are rare. One case[61] was without other neurologic disturbance and came on in the third week of illness and ended with complete recovery in three months; in the second case palsy occurred on the fifth day of illness and persisted for one year. This latter patient had normal spinal fluid. One case of Median nerve palsy has been reported.[17]

In regard to central nervous system infectious mononucleosis, it may be concluded that: because of the protean manifestations and the delayed development of a positive heterophile reaction or the lack of its presense in the serum, abnormal spinal fluid findings may be misleading: all cases of "idiopathic" meningitis, encephalitis, or polyneuritis warrant repeated heterophile antibody agglutinations for diagnostic purposes; there may be no means of establishing the diagnosis for several weeks.

Heterophile Antibody

From the foregoing and because of the multiplicity of symptoms not mentioned, it is apparent possible errors in diagnosis are numerous. However, even in those cases where the index of suspicion is high, the diagnosis of infectious mononucleosis cannot be made by clinical history and examination alone.

Stevens, Bayrd and Heck,[23] in their recent survey of 210 sporadic cases, found that 13 different diagnoses were made on admission, of which the diagnosis of infectious mononucleosis was suggested in only 7.1 per cent. The report of Davidsohn et al[62] further illuminates diagnostic difficulties. One hundred six patients with infectious mononucleosis were seen and in 63, prior to the availability of hematologic and serologic findings, 26 diseases other than infectious mononucleosis were diagnosed.

The importance of blood smear studies has been mentioned and is emphasized. This will undoubtedly solve the problem in a high per cent of cases, especially when combined with the heterophile antibody test. However, there will remain a small group of cases in which the diagnosis will rest heavily on the results of the heterophile antibody reaction alone. These cases may be atypical in onset, atypical in their course, or present differential diagnostic problems in which the blood changes are not entirely satisfactory for purposes of classification.[63] From this standpoint it is well to know something of the limitations and possibilities as regards this test.

In 1944, Kaufman[64] stated that "the percentage of positive heterophile antibody tests varies with all series reported according to (1) figure which the author considers necessary for this test to be called positive, (2) the frequency of the blood sampling in an individual case, and (3) most important, the number of cases of infectious mononucleosis which the author refused to recognize and include as such because they have a negative heterophile antibody reaction even though they are indistinguishable from

infectious mononucleosis clinically and hematologically . . . on this basis reports vary from 40 per cent to 100 per cent positive."

That a negative test does not rule out the disease is now fairly well accepted. Conversely, a positive test, if in high titer, is strong evidence in favor of infectious mononucleosis; but the borderline or only moderately elevated titer does not definitely establish the diagnosis.

In the years since 1932 when Paul and Bunnell[65] first noted a high heterophile antibody titer in infectious mononucleosis, most authorities have gradually recognized 1:56 (Davidsohn technique) or a rising titer as positive. On this basis it has been noted[64] that positive reactions may occur as early as the second or third day of illness and as late as six months, and that the average is between the sixth and the 26th day; it may remain positive for three to 11 months, averaging two to four months; the titer bears no relationship to the severity of the disease; high titers often occur following horse serum infections.

However, in recent years there has crept into the literature indication that titers up to 1:224 and even higher, in rare cases, may occur in various diseases other than infectious mononucleosis. Schultz[66] found titers of 1:56 or higher in 57 cases, which included Hodgkin's disease, monocytic leukemia, several sarcomas, and tuberculosis. It is noted that a high per cent of these titers were not above 1:112 (and that the Davidsohn differential test was not used).

One case of monocytic leukemia with a heterophile antibody reaction of 1:16,384[67] has been reported. S. Bornstein[68] has reported a case of bacterial infection with B. coli in which a heterophile antibody reaction of 1:1600 was obtained. (However, this antibody was the Forssman type.)

That the test does have a high degree of specificity was shown by the study of Goldman et al.[69] Eight hundred seventeen heterophile agglutination tests on 556 patients were done; these included 43 cases of infectious mononucleosis, 55 cases of miscellaneous lymphomatous diseases, and 458 unspecified cases. Of the unspecified cases only 10 per cent had titers of 1:80 or above; of the 55 lymphomatous cases four patients had tests in the borderline range, 1:80 and 1:60; of the 43 infectious mononucleosis cases, 98 per cent had titers of 1:80 or above and 81 per cent (35 patients) had titers of 1:300 or higher.

However, perhaps because of these occasional cases not found to be infectious mononucleosis, but with titers in what has heretofore been considered the low diagnostic range, Davidsohn et al[62] have recently suggested that a titer of 1:224 be considered "positive." They add that "if the titer is less than 1:224 in the presence of clinical and hematologic findings suggestive of infectious mononucleosis, or if the titer is 1:224 or higher in the absence of clinical and hematological findings suggestive of infectious mononucleosis, or if the patient has a history of a recent horse serum injection, the test should be checked by the differential test."

It will be remembered that according to present-day concepts there are three types of sheep cell agglutinins:[64] (1) those in normal serum (or sera of persons with diseases other than infectious mononucleosis or horse serum sensitization) absorbed by guinea pig kidney but not by beef erythrocytes; (2) those in patients with infectious mononucleosis absorbed by beef erythrocytes but not by guinea pig kidney; (3) those in the serum of individuals treated with horse serum, absorbed by both guinea pig kidney and beef erythrocytes.

Davidsohn et al[62] estimate that by use of this test in questionable cases serologic accuracy will range from 80 to 85 per cent; that if all or almost all (more than 90 per cent) of the sheep cell agglutinin is removed by guinea pig kidney, infectious mononucleosis is excluded; that failure to use the differential test has been responsible for much of the discrepancy of reported incidence of positive titers and confusion regarding the significance of the heterophile antibody test.

It is concluded that the differential test should be used on all atypical cases diagnosed as infectious mononucleosis, in the presense of hepatitis, "idiopathic" central nervous system or peripheral nerve lesions, or where the heterophile antibody titer is positive but the diagnosis is in doubt.

Conclusion

Experience, through the years, has led us to think of infectious mononucleosis as the "medical student's disease," transitory in character and of no great significance except for its nuisance value, either in the acute stage or from the standpoint of possible long-term illness. So-called ordinary typical cases probably fit this concept, and many cases mistakenly diagnosed probably settle themselves without important consequences. However, there is growing evidence that infectious mononucleosis is a protean disease of considerable magnitude; that it also is an "imitator" disease; that serious complications can occur in the acute stage and that the last word has not been written in regard to possible chronic effects; that even so-called "ordinary cases" should be viewed with suspicion and observed and studied for longer periods. The etiology is still unknown but, clinically at least, there appears to be some relationship to many established and so-called virus diseases.

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PRESIDENT'S PAGE

Dear Doctor:

The mundane affairs of everyday existence become less frenzied during this holiday season. Problems of survival and of economics and problems of war and of government melt, even if ever so briefly, while our thoughts turn toward the Bethlehem star.

So in the place of my usual concern over the troubles besetting us, may I devote this space toward wishing each of you a Merry Christmas and Glorious New Year.

Sincerely,

EDITORIAL COMMENT

Executive Assistant for Society

The Kansas Medical Society is pleased to announce that an addition has been provided in the office. This new position, known as that of executive assistant, will enable the Society to expand its public relations as well as its other operational activities.

The Council acted to create this new position about six months ago. During the interval since that time, some 15 persons applied, and after references were received this field was narrowed to three. The final decision was made by the Executive Committee after personal interviews.

On December 1, 1952, Mr. Rueben Dalbec began his work with the Society as executive assistant. Mr. Dalbec is of Swedish and German descent and comes originally from Wisconsin. He is 28 years old, a veteran of three years service with the Coast Guard, and a graduate of the University of Wisconsin. Prior to this position, Mr. Dalbec was manager of the Student Union Building at Washburn University. He organized this important campus activity and comes to the Society with highest recommendations from the president and the faculty at the university.

Mr. Dalbec is married and has two children, ages nine and five. Prior to his coming to Topeka, he was the assistant manager of the Student Union Building at the University of Wisconsin. His avocation is music, in which he has achieved professional recognition, having at one time written and directed the Miss America Pageant at Atlantic City.

Mr. Dalbec will assist the executive secretary in all the different Society functions and will give to the Society the advantage of an additional person to carry out its expanding public service program.

Medicine's Political Responsibility

On November 4 the American people voted a political change in their policy of federal government. While this will affect various activities in many fields, the election has also altered the subject of health care for the people of this nation. This difference has been variously expressed by different people, but perhaps the shortest and the most accurate evaluation is that medicine will now face a direct responsibility toward the practical solution of existing health problems.

Expanding that statement slightly, it will be recalled that during the past few years the consumer of health services has dominated the picture, relegating the physician into the role of critic. It now becomes medicine's responsibility to explore the health needs of this nation, to correct public opinion where it is in error, and to correct deficiencies in service where they exist. The difference will lie in the fact that today medicine has an opportunity of providing this answer along lines that are scientifically sound. Therefore, it appears that the crisis of medicine is not less acute than before, that on the contrary the physician faces an enlarged obligation. He is, however, provided with an opportunity to justify his position. In that role it appears that no single effort should be relaxed, but that practical and appropriate solutions must be found for those problems the public is asking to have solved.

The opportunity presents itself because of the stand taken by Mr. Eisenhower and the Republican Party on medical issues. It is well known that Mr. Eisenhower is opposed to socialized medicine and to compulsory health insurance. This, however, has not solved the public clamor for some means whereby the cost of catastrophic illness may be amortized nor does it provide an adequate supply of physicians to all sections of our nation.

Mr. Eisenhower is determined that medical education shall be provided without resorting to federal financial assistance. Here again the challenge rests with the medical profession, because medical education must find some means of becoming solvent. The general has also promised a firm assessment of the Veterans Administration's medical care program, but unless a sound plan can be developed, the end result certainly will not be an improvement on the present situation.

And there are many more issues upon which the new president and the party he represents have stated that they expect to take action. The course that will be taken depends upon the soundness and the effectiveness of the advice given them by the profession itself. That represents in outline an explanation of the earlier statement declaring that medicine's obligation today is greater than ever before.

American Medical Education Foundation

A renewed effort to stimulate gifts to the American Medical Education Foundation, in the hope that contributions may total one million dollars by January 1, 1953, is now being made by the American Medical Association. Individual solicitation is being conducted by direct mail, but a reminder is printed here to call the attention of Kansas physicians to their obligation of supporting the future of medical education.

The need for such support is obvious. Physicians, as a group, have resisted efforts of the government to provide federal funds for the purpose, thereby

implying that money could and would be obtained from other sources. They have inaugurated a program for collecting those funds, and now need only individual action from the membership of the A.M.A. to prove that the profession is interested in its own future.

From a selfish point of view, a physician can also find reasons for generosity to the Foundation. The income tax scale for 1952 is the highest it has ever climbed, and business men assert that years of high taxation are years in which contributions can be made most economically. Contributions to the Foundation are deductible up to 20 per cent of taxable net income.

The net cost of gifts to the Foundation must be computed on an individual basis. An example, however, will illustrate the effect. A married physician who has two children, whose contributions are 10 per cent of his adjusted gross income of $5000, could give $1000 to the Foundation and would thereby be eligible to deduct $222 from his tax payment. If his income and contribution were doubled, his tax saving would be $492. Those whose adjusted gross income totaled $20,000, could contribute $4000 and realize a tax saving of $1340.

Kansas cannot compete with more populous states in the amount of its contribution, but Kansans individually have it in their power to raise the per capita gifts to a level of which we can be proud. The Kansas Medical Society endorses this project and hopes that physicians will send checks in generous amounts before the end of the year. The address to be used is American Medical Education Foundation, 535 North Dearborn Street, Chicago 10, Illinois.

Medical Board Reports

A report from the Kansas State Board of Medical Registration and Examination was made to the Hon. Edward F. Arn, Governor of Kansas, on November 1 by Dr. O. W. Davidson, secretary. The Journal thought it was of interest to the profession to obtain statistical information regarding the physicians of Kansas, and therefore requested Dr. Davidson's permission to publish the report which follows.

* * *

It is my privilege to present a report upon the activities and status of the Kansas State Board of Medical Registration and Examination for the period of July 1, 1951, to June 30, 1952.

We have at present 3,091 licensed physicians on our records; of this number 1,950 are located in Kansas. The out-of-state registrations include 151 who are at present in military service and exempt for such period of re-registration fee. Our in-state registration gives us a per-capita ratio of about one physician for every 1,000 persons in Kansas. This places Kansas in a very favorable position in the per-inhabitant ratio of the states of the union.

Since we now have no established reciprocity system with other states in the matter of exchange of licensing, we may recognize the license of any other state whose preliminary qualifications are the same as or equal to ours, and who extend the same privileges to our licensees, provided they have received their license by examination and not through reciprocity with some other state. Diplomates of the National Board of Examiners may, at the discretion of our Board, be licensed without further examination.

Graduates of foreign medical schools may be licensed if they produce proof of U. S. citizenship and board-acceptable qualifications. All such applicants are required to take the written examination. Foreign graduates, with potential qualifications for examination, may be issued Fellowship Certificates for rights to practice in state-governed hospitals if they are accepted for training and service in such institutions. Five such fellowships have been issued during the fiscal year just past and 99 inquiries from foreign doctors have been received and answered.

During the period covered by this report, the Board has issued 183 licenses, 90 by examination and 93 by endorsement. Four applicants failed to pass the written examination. Twenty-four failures of licensees to pay the annual re-registration fee resulted in cancellation of their rights to practice medicine in Kansas. All of these were out-of-state, except eight, who have forfeited their rights also. Reinstatements were made by 38 who produced evidence, satisfactory to the Board, concerning their ethics, moral and professional conduct. Sixteen licensees were lost by death and five by retirement. Fifty-two temporary permits were issued during this period, to applicants with acceptable qualifications which gave them the right to practice until the next regular Board meeting when their applications were confirmed. One hundred sixty-nine inquiries from the Bureau of Narcotics were received and answered concerning the status of physicians.

All inquiries concerning professional conduct were followed up and resulted in one or more personal conferences with the secretary and attorney for the Board. In 15 instances, hearings were held before the entire Board. In two instances, physicians accepted recommendations that they suspend practice in Kansas until they had satisfactorily corrected habits that made it undesirable for them to practice. In co-operation with special committees of the Kansas Medical Society, grievances have been settled, in many instances, without publicity or embarrassment to anyone. Through such co-operation with the Kansas Medical Society and the University of Kansas School of Medicine at the student level, much is

being accomplished to promote good public relations and provide Kansas with competent doctors of medicine.

The annual registration notices were sent to 3,400 physicians; second notices were necessary for 239. During the year 100 endorsements were executed on applications to other states, and six duplicate licenses were issued to replace those legitimately lost or destroyed. Approximately 200 communications were handled by the attorney for the Board in addition to an average of 15-20 daily communications by the secretary's office. Congratulatory communications were sent to all physicians who received newspaper or medical journal publicity for 40 or more years of service to the public.

In addition to full attendance at four Board meetings, during the period of this report, three members of the Board represented Kansas at the annual meeting of the National Federation of Medical Examining Boards in Chicago, Illinois.

The fee for license by examination in Kansas is $25; license by endorsement from another state is $50 or equivalent to the amount that state charges a licensee from Kansas. The annual re-registration fee is $1.00; the reinstatement fee is $5.00. A fee of $10 is charged by the Board for endorsement of applications to other states, rendering a duplicate license or issuing a temporary permit. All collections are sent to the Kansas state treasurer, where 10 per cent is transferred to the general fund. All expenditures of the Board are paid by voucher on the state treasurer. Our records are audited annually by the state auditor. The secretary and clerk of the Board are bonded. Total amount collected for the period of this report was $12,751; total amount disbursed during that period was $12,268.82.

Respectfully submitted,

O. W. Davidson, M.D., Secretary.

Kansas Division, A.C.S., Elects

Dr. Charles H. Miller, Parsons, was named president of the Kansas Division of the American Cancer Society at a meeting held in Topeka last month. Other officers elected are: vice president, Mrs. Tom Stewart, Wellington; secretary, Mr. J. W. Kirkpatrick, El Dorado; treasurer, Mr. Robert A. McClure, Topeka; chairman of executive committee, Mr. A. H. Saville, Topeka; executive director and assistant secretary, Mr. W. Miles Pulford, Topeka.

Service Separations

As a service to physicians and communities in this state desiring additional medical personnel, the Journal of the Kansas Medical Society will publish in this column each month the names of medical officers who will shortly be separated from the armed forces. These are men who volunteered from Kansas, and many of them will probably be interested in finding locations in this state. Anyone interested in contacting these physicians may write to the address here given.

Niles A. Borop, Jr., M.D.
U. S. Army Hospital
Camp Carson, Colorado

Frank C. Brosius, Jr., M.D.
126 South Fountain
Wichita, Kansas

Bernard A. Brungardt, M.D.
137 North 9th Street
Salina, Kansas

Herbert Bunker, Jr., M.D.
U. S. Army Hospital
Fort Riley, Kansas

Eran O. Burgert, Jr., M.D.
2620 East Waterman
Wichita 7, Kansas

James H. Enns, M.D.
211 S. E. 4th
Newton, Kansas

Mayer Fisch, M.D.
Winter VA Hospital
Topeka, Kansas

Charles C. Gilkey, M.D.
1731 Clay Street
Topeka, Kansas

Charles R. Hopper, M.D.
172 Artillery Loop
Fort Sam Houston, Texas

Edwin R. King, M.D.
1708 First Street, N.W.
Washington 1, D. C.

Robert V. Kirk, M.D.
248 West 12th Street
Horton, Kansas

David Lukens, M.D.
129 West 19th Street
Hutchinson, Kansas

Ward A. McClanahan. M.D.
1425½ Buchanan
Topeka, Kansas

Arthur W. McMahon, Jr., M.D.
Winter V.A. Hospital
Topeka, Kansas

Don R. Miller, M.D.
1847 Oakland
Kansas City, Kansas

Max E. Musgrave, M.D.
Denton, Kansas

William J. Reals, M.D.
Wichita Hospital
Wichita, Kansas

Joseph E. Seitz, M.D.
Wakeeney, Kansas

Dana A. Tompkins, M.D.
Route 2
Bonner Springs, Kansas

Richard C. Tozer, M.D.
Winter V.A. Hospital
Topeka, Kansas

Harold M. Voth, M.D.
2115 West 10th Street
Topeka, Kansas

John L. Weaver, M.D.
4206 Prairie Lane
Mission, Kansas

Robert Weimer, M.D.
206 Third Street
Fort Leavenworth, Kansas

George A. Westfall, Jr., M.D.
Hertzler Clinic
Halstead, Kansas

Lyle E. Wonderlich, M.D.
612 Eighth Street
Concordia, Kansas

Case Reports from the University of Kansas Medical Center Tumor Conference*

Germinal Tumors of the Testis

Edited by Harlan I. Firminger, M.D., and Floyd R. Skelton, M.D.**

Dr. Helwig: Today we have three cases of testicular tumor, forming a nucleus for discussion of the prognosis of such cases and the pathologic, surgical, roentgenologic and endocrinologic aspects of the problems which testicular tumors present. Dr. Stockton, would you present the histories in these three cases, and then we will proceed to the discussion.

Case No. 52-104

Dr. Stockton: A 44-year-old minister was admitted to the hospital in June, 1950, complaining of low back pain, fever, anorexia and weight loss. Twenty-four years previously he spontaneously developed pain, swelling and increased temperature in the right scrotum. These inflammatory symptoms subsided in about 10 days, but the swelling and the firmness persisted, and the testicle continued to become slowly larger throughout the years. About two years ago the patient again started having aching pain in the right testicle and some back pain. This finally became so severe that he sought medical aid at another hospital in 1949.

The diagnosis of a probable neoplasm was made and an orchiectomy performed. The patient was advised that the tumor was carcinoma, and subsequently he received 37 x-ray treatments. He remained asymptomatic from November, 1949, until April, 1950, when weakness, fever and low back pain recurred. By the time of admission to this hospital in June he had lost approximately 15 pounds since his orchiectomy. He also complained of a recent non-productive cough and a feeling of fullness in his throat. The man did not look particularly ill, but he was extremely nervous. The striking thing on physical inspection was a fullness in the suprasternal notch with dilatation of the superficial veins in his throat. When he turned his head it was easy to note a large supraclavicular node on the left. Examination revealed a smaller node in a similar position on the right. His right testicle was absent but there was no induration, tenderness, or evidence of local recurrence.

Could we have the x-ray findings on this man?

Dr. Litton: Roentgenograms of the chest revealed a circumscribed mediastinal mass involving the hilar and peritracheal lymph nodes on the right, and, to a lesser extent, on the left. This was interpreted as undoubtedly a metastatic mass. A lateral film of the spine strongly suggested metastasis involving the pars medialis and the base of the spinous process of the fifth lumbar vertebra. It was felt that this patient had widespread metastases from the previously removed tumor of the testicle.

Dr. Stockton: Because of these roentgenological findings and the presence of the enlarged supraclavicular nodes, we felt that he had rather widespread metastases from the tumor of the testicle and we advised x-ray therapy, which he received as an outpatient. I have not heard from the man, but the Tumor Registry has ascertained that he died in June, 1951.

Case No. 52-105

The second case is that of a 38-year-old white man, who was admitted to the hospital on May 12, 1950, complaining of a recurrence of aching pain and swelling in the right groin of 4½ months duration, following surgical removal of his right testicle in November, 1949, at another hospital. The patient stated that he had had an aching pain in his right scrotum and enlargement of the testicle approximately three years before. He did not seek medical advice at that time and, in fact, did not do so until the testicular enlargement was approximately the size of an orange and causing him considerable discomfort. His local doctor then did a right orchiectomy and advised him that the tumor was cancer, Grade IV. The patient was asymptomatic following surgery until January, 1950, at which time he again developed aching pain and swelling in the right groin. He entered this hospital on the advice of his local doctor.

Physical examination was essentially negative except for a hard, nodular, semi-fixed mass approximately 2 x 5 cm. overlying the pubis just to the right of the penis. The mass extended deep into the soft tissue and was moderately tender to palpation. Laboratory studies were within normal limits. X-rays of the chest, kidneys, ureters and bladder were considered normal.

On May 13, 1950, the patient was taken to the operating room, where a high inguinal incision was made and the right spermatic cord ligated and severed before removal of the carcinomatous recurrence

*Cancer teaching activities aided by a training grant from the National Cancer Institute, U. S. Public Health Service, and the Kansas Division of the American Cancer Society.

**Trainee of the National Cancer Institute.

in the stump of the cord. This lesion was grossly neoplastic and was dissected *in toto*. The scrotum was invaginated and all scar tissue excised. Dissection was carried retroperitoneally along the iliac vessels, but no node involvement was discovered. Postoperatively the patient developed a thrombophlebitis in the right leg and was placed on heparin and dicumarol therapy. X-ray therapy was started on June 9, 1950, and the patient was dismissed on June 16, to continue x-ray treatments as an outpatient. The pathology report on the surgical specimen was embryonal carcinoma with foci of necrosis and hemorrhage. A report from this man's local physician states that he died on March 3, 1951.

Case No. 52-106

The third case is that of a 44-year-old man, admitted with the complaint of a moderately painful mass in the left upper quadrant and loss of approximately 30 pounds of weight in the previous two months. His history revealed that 15 years prior to admission he had had a left orchiectomy for a tumor mass, which had been reported at this hospital as alveolar sarcoma. He received x-ray therapy and was completely asymptomatic from 1937 until about 18 months prior to this admission in 1952. When symptoms of backache and some weakness recurred, he consulted a doctor in Texas, who said that his left kidney was ptotic and did not drain properly. The pain became more severe. Shortly thereafter he noticed the development of a mass in the left upper quadrant and he came to this hospital, bringing intravenous pyelograms which showed a non-functioning left kidney.

On physical examination the only positive finding was a large, hard, non-tender mass in the left upper quadrant of the abdomen extending from the rib margin to the iliac crest and a little to the right of the umbilicus. He was given x-ray therapy for eight days with no apparent diminution in size of the mass, so he was admitted to this hospital for further evaluation and possible surgical treatment. Findings on admission were essentially the same, and laboratory studies were negative except for 75 per cent hemoglobin and elevation of the sedimentation rate to 25 mm. in one hour.

Could we see his x-rays, please?

Dr. Litton: The roentgenogram of the chest is essentially normal, but retrograde pyelograms (Figure 1) reveal a deformity of the lower pole of the left kidney and upper third of the left ureter. This was interpreted as hydronephrosis, probably due to an obstruction from a neoplasm. This could be the result either of metastatic involvement of the lymph nodes surrounding the ureter, or possibly a primary tumor involving the left ureter.

Dr. Stockton: He was taken to surgery on July 19 of this year, and a mass was found which occupied almost the entire left retroperitoneal gutter, involving the vascular pedicle of the left kidney and the ureter so hopelessly that it could not be dissected out. Because of the hydronephrosis and the possibility of pyelonephritis with attending sepsis, it was felt that as a palliative measure it would be worthwhile to take out the kidney, which was done. A biopsy was taken of the mass, which later proved to show only acute and chronic inflammatory fibrous tissue. We felt, however, that this was a metastasis from the tumor of the testicle which had been removed 15 years earlier, and he was given x-ray therapy prior to dismissal. This patient has not been back for a checkup, and as far as I know we have no follow-up on him.

Dr. Helwig: Did he have any regression in the retroperitoneal mass following his x-ray therapy?

Dr. Tice: He got relief from pain and felt better.

Dr. Helwig: I think the whole problem we see here is unique; for a patient to go for 15 years and then have a recurrence along the distribution of the spermatic vein is an unusual story. The fact that we could not establish the presence of any tumor histologically further clouds the picture. How big was the mass that you removed by biopsy?

Figure 1. Case No. 52-106. Retrograde pyelogram reveals dilatation of the renal calyces and upper part of the ureter on the left with irregularities and distortion of the left ureter suggestive of compression by a surrounding tumor mass or direct involvement of the ureter by tumor.

Dr. Stockton: It was a very small piece.

Dr. Tice: Do you think you missed the tumor, or do you think the biopsy tissue was representative of the tumor?

Dr. Stockton: I think I missed the tumor.

Dr. Helwig: Do you think inflammatory tissue would account for this mass, Dr. Tice, or did you feel you were actually dealing with a local tumor recurrence?

Dr. Tice: There was a question in my mind. The retrograde pyelograms revealed a large mass. I interpreted it as a recurrence of the testicular tumor or a primary kidney tumor.

Dr. Helwig: Dr. Stoddard, would you show the pathologic findings on these three cases, please?

Dr. Stoddard: Testicular tumors present a field of diagnosis in which there is room for difference of opinion and, furthermore, there has been a great deal of variation in the terminology that has been applied to the same tumor. According to our presently accepted terminology, I think we can consider that these are three instances of seminoma. In the first two cases, you will recall, the orchiectomies were done at other hospitals and I have nothing to tell you about the gross specimens. In the second case, approximately 10 months before death a length of spermatic cord and a 5 x 5 x 4 cm. gray homogeneous tumor mass were removed in this hospital. In the third case, we do not have available at this time the report on the specimen removed 15 years ago, but we do have a histological section from that specimen. In addition, we have the kidney and the biopsy that turned out not to be neoplasm which were removed at operation in July, 1952.

Histological sections in the first two cases are essentially identical. Each reveals a tumor remarkably uniform in its cytological composition with areas of necrosis characteristic of seminoma. The tumor is composed of rather poorly defined cords of cells. The cells are quite uniform, with abundant pale cytoplasm, often with the cellular outline indefinite, and round vesicular nuclei containing a nucleolus. In the stroma there are small lymphocytes often seen in seminoma. Both of these tumors contain a moderate amount of fibrous stroma (Figure 2). One must always be on the lookout in testicular tumors for variation from area to area, and I looked at the material we have with some diligence without finding such variation.

Figure 2. Case No. 52-104. A representative area of dense fibrosis seen in many places in both the first and second cases. A small amount of the seminoma is evident in the lower part of the picture and along the right margin. Hematoxylin and eosin. X 110.

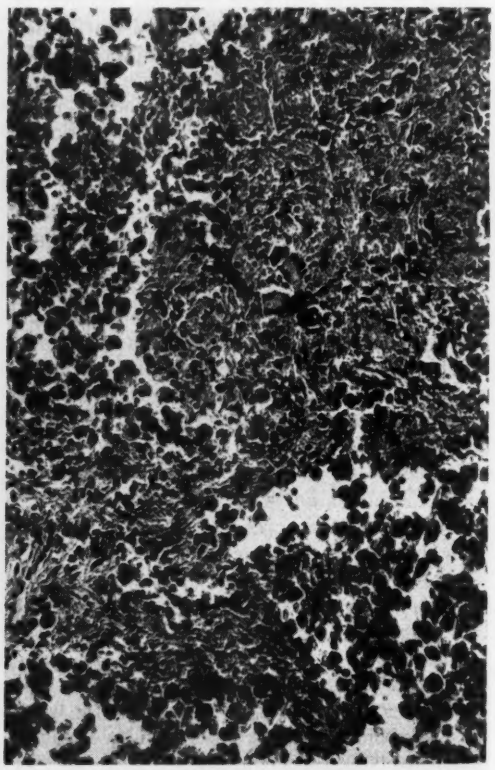

Figure 3. Case No. 52-106. Granulomatous focus with prominent multinucleated giant cells. Surrounding seminoma contains a small amount of lymphoid stroma in this area. Hematoxylin and eosin. X 190.

In the third case, the tumor has almost all the histological features that have been described in seminomas. The cells are much the same, and they are arranged in the same kind of grouping. Once more we have lymphocytes in the stroma. In addition, there are little areas in the stroma showing a granulomatous type of proliferation (Figure 3). The kidney shows the changes characteristic of pyelonephritis and, I think, too, some atrophy, perhaps because of compromising of the renal artery by the mass around it. The small biopsy specimen was composed only of fibrous and inflammatory tissue.

Discussion

Dr. Helwig: It is rather interesting in the first two cases that these patients went such a long time before they had anything done, and that is a common story. I think in almost 700 cases of undescended testis that the Leahy Clinic[1] had, the average duration before diagnosis was approximately 15 months, because patients usually do not have local pain and discomfort early.

I would like to re-emphasize what Dr. Stoddard said about classification of these tumors. Up until the large amount of material was studied from the Second World War—I think well over 1000 cases, perhaps considerably more—at the Armed Forces Institute of Pathology,[2] there was no meeting of the minds apparently on nomenclature, particularly since some, following Dr. Ewing, left out the old diagnosis of seminoma and referred to them as embryonal carcinoma with or without lymphoid stroma. However, I believe this new classification—it's not new, but it's worked out on rather large amounts of material, you must admit—of the adult teratoma, the seminoma, the embryonal carcinoma, the teratocarcinoma, and the choriocarcinoma, more or less fits in with our ideas.

Dr. Firminger: I would like to report on the sequel to that work you refer to, Dr. Helwig. The lack of adequate follow-up information on these cases was the greatest deficiency of the report by Friedman and Moore[2] in the memorial issue for Colonel Ash in the *Military Surgeon* back in 1946. Subsequently, Dixon and Moore[3] followed up these cases, and now have information on almost all for at least two years and, in many instances, for five years.

Dixon and Moore analyzed 894 primary germinal tumors of the testis; 536 of them were "pure" and 358 were mixed. By "pure" they meant tumors in which on all the sections they examined, which were usually several, they found only one histologic type. Their results show "pure" choriocarcinoma is a rare tumor and constitutes less than one per cent of testicular tumors; seminoma, on the other hand, is the most common type of "pure" germinal tumor. In their analysis of the mixed variety, seminoma was found in 34 per cent, embryonal carcinoma in almost 90 per cent, choriocarcinoma in about 8 per cent, and so on. So you can see what a mixed mixture there can be.

When the histologic types are analyzed as to mortality, the pure seminoma has a low mortality; only eight per cent dead in two years and 11 per cent dead in five years. As is true of all the germinal tumors, about 90 per cent of the patients who are going to die within five years are dead in two years. So a two-year follow-up is actually a fairly satisfactory follow-up for testicular tumors of the germinal type. Although pure seminoma has the lowest mortality, when it is mixed with other tumor types it does not appear to lower the mortality. Interestingly, the study of Dixon and Moore revealed that when embryonal carcinoma begins to form teratomatous elements, the mortality is markedly improved; and when it differentiates completely to the adult type, the mortality is even further improved. Dixon and Moore explain the still sizable mortality of adult teratoma by metastasis occurring before this tissue has differentiated; however, they admit that their examination was not adequate to rule out possible concurrent presence of embryonal carcinoma.

The study of Dixon and Moore has gone still further; and since we are primarily interested in seminoma in this conference, I might give you some information that they gathered on seminoma. They examined their group of seminomas to see if they could find any histologic differences that were significant. They classified all the things they could recognize in seminomas and put the data on punch cards. They analyzed such things as the incidence of mitotic figures, the size of the cells, the presence of fibrosis, the presence of eosinophils, the presence of lymphoid stroma, the presense of necrosis, the presence of hemorrhage, vascular invasion, lymphatic invasion, the presence of a granulomatous reaction, and things of that sort.

Then they analyzed the punch cards for all these different elements and found that five of these histologic findings were significant in relation to mortality. The figures that they reported in Paris showed seminomas with lymphoid infiltration had a mortality of only four per cent. If there was no lymphoid infiltration of any notable degree, the mortality went up to 16 per cent. If there was infiltration by eosinophils, the mortality was only three per cent; if there was no eosinophil infiltration, the mortality, according to them, was 11 per cent. Stromal response appeared to be bad, because if there was no stromal response there was only seven per cent mortality; but if there was stromal response,

in the sense of fibrosis, such as we saw in these first two tumors, the mortality was 19 per cent.

The presence of vascular invasion, as seen in the ordinary hematoxylin and eosin sections forebode a much higher mortality than any of the other factors. The presence of granulomatous reaction was one of the best things one could find, and the mortality went down to three per cent. Interestingly, granulomatous reaction was present in the third case, the man who has lived 15 years.

I think some question arises as to what constitutes lymphoid infiltration or the absence of lymphoid infiltration, but it is interesting that these cases would seem to agree with Dixon and Moore's statistical findings, because in both patients who died soon there was a fair amount of fibrous reaction (Figure 2). In the case that survived, there was this granulomatous reaction (Figure 3), and in one portion of the section there was actual lymphoid tissue, both apparently prognostically favorable findings.

Dr. Stoddard: How was variation in treatment taken into account in this series?

Dr. Firminger: Fairly well. Dixon and Moore said that 89 per cent of the patients were treated by surgical excision and postoperative x-ray. Unfortunately, they did not throw out the five per cent who were treated by surgery alone and those who were treated by radiation alone; but the 89 per cent treated similarly—I say similarly with my tongue in my cheek, because they were not treated by the same individuals, but treated at least by orchiectomy and postoperative x-ray—would add some uniformity and some validity to the figures.

Dr. Helwig: Dr. Firminger, would you care to comment on bioassay in this group of neoplasms?

Dr. Firminger: The bioassay studies that were done on this group of tumors that you referred to from the Armed Forces Institute of Pathology were done at such varied places and so non-uniformly that they were not worth much. However, some very interesting studies were done by Hamburger,[4] in which he found a high correlation of secretion of pituitary follicular-stimulating hormone, FSH, with cases of seminoma. In cases of teratocarcinoma and the mixed type of tumors of the testis, there tended to be chorionic gonadotropin in the urine. These findings were not diagnostic, and there were many cases of tumors that did not show either hormone. The finding of FSH in cases of seminoma was apparently due to the castration effect of the tumor rather than secretion by the tumor itself; it was no higher than the level found in hemicastrated individuals. On the other hand, it was thought that the chorionic gonadotropin might well originate in the testicular tumor, and Hamburger and others have shown that when one finds chorionic gonadotropin in the urine the prognosis is poor.

Dr. Helwig: Would you like to comment on the survival rate of the choriocarcinoma?

Dr. Firminger: I am not prepared to give any definitive information on the survival rate of cases of choriocarcinoma except to say that it's probably the worst testicular tumor that we have and it approaches 100 per cent mortality.

Dr. Helwig: Thank you, Doctor. In the early days of the study of testicular tumors, some of you may recall that Ferguson[5] at Memorial did a great deal of work on bioassay, and he led everybody pretty much astray as to what he felt he was able to do in histologic type with simply gonadotropin determinations in the uterine muscle of the mouse. He went so far that it almost became ridiculous, because at that time they were treating the lesion locally with radiation and then taking out a "batch of soup," and pathologically you often didn't know what the tumor was. But this more recent work has, I think, cleared up this misunderstanding.

Dr. Schloerb: I would like to ask a question about the FSH assay. Is this a postoperative assay, or preoperative? In other words, did the patient have one normal testis?

Dr. Firminger: The patients did have one normal testis. I'm not quite sure what the division was on the preoperative and postoperative basis.

Dr. Helwig: I know you are all familiar with Michalowsky's[6] original experiments of inducing teratomas in the testis of the rooster with zinc chloride. And then Halsey Bagg[7] came along and saw that when the rooster's wattles are nice and red and he is ready for the springtime, you could induce these tumors with great ease, whereas if you waited till the winter months when his comb and wattles began more or less to droop, you had no success. However, with the use of anterior pituitary hormone he could produce testicular teratomas at any time of the year in the rooster.

Another point of interest is the relationship here to cryptorchidism. In one series of 694 cases of cryptorchids,[1] 11 per cent had carcinoma, which is about 48 to 50 times as frequent as the incidence in the general male population. Further, in the case of a single cryptorchid, if a tumor occurred, in approximately 98 per cent it occurred in the cryptorchid testis, and not in the normal testis; whereas if a tumor developed in a case of bilateral cryptorchidism, there was a 25 per cent chance that the tumor would be bilateral. So with those striking figures, I think we must admit that there is some etiologic relationship in undescended testes to the development of a malignant tumor. It used to be

thought that this was apparent rather than real, but a careful study, I believe, has borne out its reality.

There are two points in therapy that I think are worth discussing. There seems to be a mild difference of opinion—or maybe there was, maybe that's all been settled now—regarding the extent of the surgery before irradiation is done, whether you go up and try to do a big job or simply get as much of the cord as you can, and then start your x-ray. So I am going to ask you, Dr. Stockton, to discuss the surgical aspect; and then I'll ask Dr. Tice to talk about x-ray. Would you mind commenting, please?

Dr. Stockton: In the reports of treatment of these tumors in the urological journals there have been a number of articles concerning very small series really, as to the proper treatment, whether simple excision or simple excision plus lymph node dissection; all are followed by radiation of course. There is no question in anybody's mind but that the spermatic cord should be ligated high, that is, at the internal ring, before any manipulation of the tumor. And that is the procedure in most hospitals. But we still see a lot of patients who come in, where their local physicians have taken the testicle out through an incision in the scrotum, which we feel is the wrong thing to do. The literature is in agreement on that.

Now whether there is any need for radical retroperitoneal dissection, I find hard to answer. Merren, Vest and Lupton[8] reported a small series of cases in which simple orchiectomy was done, that is, the high ligation, followed by x-ray therapy, with a 53 per cent survival. They had followed those patients from two to 23 years. And then there is a series, I think of 45 cases, done by Lewis,[9] in which he did orchiectomy plus what he termed a radical dissection, followed by x-ray therapy, and had only a 35 per cent survival. He had followed those patients only a year and a half to five years.

I, myself, rather have the feeling, depending on the individual case, the history of how long this tumor has been there and the preoperative findings, that high ligation of the cord, removal of the testicle, and x-ray therapy is probably going to give us as good a result as a radical lymph node dissection. There is another thing that I think is important, especially in cases of seminoma, because they have a much better prognosis than the other malignant tumors of the testicle. I think there have been reported anywhere from 55 to 65 per cent five-year survivals. I think that one shouldn't doom a man even with metastatic lesions. I have seen reports of two cases[8] that had pulmonary metastases, one of whom received only x-ray therapy with removal of the tumor, and the other man had removal of this tumor and lobectomy. Both of those patients are alive, four and seven years later respectively. So that's not an entirely hopeless situation.

Dr. Helwig: I know Dr. Pohle[10] of Wisconsin in 1938 reported a boy with multiple "snowballs" in his chest who survived around 13 years after only x-ray to the chest. I have seen no follow-up on that case, but it's always made me feel that even if they've got metastases in the lungs, it's worthwhile to treat the involved areas with x-ray.

If there is anything that has been a real triumph, to my way of looking, for radiation therapy, it's been in the management of this group of tumors. Even in my short life, I can still remember as a medical student and for many years thereafter that if in a student—and we see it frequently in medical students because that's the age at which it occurs—you made the diagnosis of testicular tumor, you told the boy to make his peace with God because he was doomed, and he was usually dead within 18 months or two years. Now, with seminoma and some of the embryonal carcinomas, it is possible to salvage by x-ray therapy and orchiectomy as much as 70 per cent of these patients for five years or longer; and if you get them by that five-year period, the outlook is pretty rosy. Hasn't that been your experience, Dr. Tice, that you get quite an insignificant number of recurrences after that date?

Dr. Tice: Of these three cases, the first one did not respond in the slightest to radiation therapy. He had had quite a lot of radiation elsewhere, so we didn't feel like extending the dose very high. He did not respond; his mass did not regress and his pain was not relieved. The last case, the man who had his tumor 15 years ago, did show definite response. We haven't had a follow-up, but we should get it soon.

One of the most interesting cases we have had was a young fellow who came in about 15 years ago with a mass in his abdomen, with a history of having had a testicular tumor removed by an osteopath. He was given radiation, on the assumption that it was seminoma. The mass regressed. He returned 18 months later and his mass was gone. He was feeling fine. I made the remark that I wished that I had a specimen, just to prove that he had had a tumor in the first place. He said, "I have it at home in a bottle on the mantle." He sent it to us, and Dr. Wahl sectioned it and reported that he had had a malignant seminoma. So we did prove our diagnosis. I have followed him now for about 15 years.

I think the important thing in treating these cases is not to limit the radiation to the pelvic lymph nodes, but to treat the periaortic nodes. I think the mistake made on the third case was that we did limit our radiation 15 years ago to the pelvis.

When he came back, he had his recurrence higher up. We give the greatest dose possible to the pelvis and also radiate the periaortic nodes and perhaps even radiate the thoracic lymph nodes. I try to get as much as 3,000 r depth dose into the periaortic nodes and into the pelvis as routine procedure. I think that they should have radiation whether there is evidence of metastasis or not.

Dr. Firminger: There is one other figure from the studies of Dixon and Moore which I would like to give you. It refers to the survival of patients that already have metastases. Apparently the size of the tumor at the time the patient is seen is not too important. The seminomas generally were larger than the other tumors, yet, as you see, the survival was better. Of the patients who had seminomas widely disseminated at the time they were seen, 48 per cent were alive two years later. That was not a hopeless condition, and Dixon and Moore attributed this to the susceptibility of seminoma to x-ray. In contrast, patients with other germinal tumors and similarly widespread metastases at the time they were originally seen had a death rate of 90 per cent.

Dr. Helwig: Would anyone like to ask any questions or comment on this series of cases?

Dr. Schloerb: Do many testicular tumors respond to endocrine administration?

Dr. Helwig: Not to my knowledge. Dr. Firminger, do you care to comment on this?

Dr. Firminger: I am hardly qualified to answer that. But I can tell you that those reports I have read in the literature are negative; although it seems logical that they should respond to hormones, none of them have.

Dr. Helwig: Any other comments?

Dr. Stockton: One other thing that I think should be brought out is that about 10 per cent of these tumors are accompanied by hydrocoele.[11] It is very important, I think, when you encounter a hydrocoele, asymptomatic though it may be—because fully 85 to 90 per cent of testicular tumors are asymptomatic except for the hardness when they start out—if you can't palpate the testicles satisfactorily through the surrounding fluid, the hydrocoele should be aspirated or excised to ascertain whether the testicle is normal.

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Eight fellowships in industrial medicine will be offered by the U. S. Atomic Energy Commission for the 1953-1954 academic year. Applications will be received until January 1, 1953, by AEC Fellowships in Industrial Medicine, Atomic Energy Project, University of Rochester, School of Medicine and Dentistry, Rochester, New York.

DEATH NOTICES

EDWARD HINMAN JOHNSON, M.D.

Dr. E. H. Johnson, 78, an honorary member and former secretary of the Maroin County Society, died suddenly on October 23 at Walton, while en route from Wichita to his home in Peabody. He was graduated from the College of Physicians and Surgeons, Kansas City, in 1902, and immediately began practice in Peabody. During World War I he served in the Army medical corps. He was active in civic as well as professional affairs, was a member of the Peabody school board for 15 years and took great interest in work with the Boy Scouts.

* * *

ROBERT HAWKINS, M.D.

Dr. Robert Hawkins, 93, a resident of Marysville for 80 years and a practicing physician there for more than 40 years, died on October 25. He received his education at Rush Medical College, Chicago. He was a member of the Marshall County Society and had held honorary membership since his retirement several years ago.

* * *

MILO GOSS SLOO, M.D.

Dr. M. G. Sloo, 73, who practiced in Topeka from 1909 until his retirement in 1948, died on November 4. He attended Topeka schools and the University of Kansas, and completed work for his degree at Rush Medical College, Chicago. After internship at the Santa Fe Hospital, he took postgraduate work in Chicago for three years before returning to Topeka to practice. He was an honorary member of the Shawnee County Medical Society.

BLUE SHIELD

A Visit to U. M. S.

A recent visit to the offices of United Medical Service in New York City re-emphasized the similarity between plans, large and small. Here is a plan operating in 17 counties surrounding the New York City area, dealing with 17,000 participating physicians, serving two and one-half million members, yet their problems and professional relations program are practically identical with those of the Kansas Plan.

This staggering number of participating physicians is not their complete list. This particular plan pays non-participating physicians on the same basis as those who participate, necessitating the listing of some 22,000 physicians. The smallness of the area makes it possible for their professional relations department to work on a much more personal basis than can be achieved in Kansas. Obviously, their professional staff is much larger. Appointments are arranged and calls made at the physician's office, as many as possible in a day.

In Kansas, most of the physician relations activity is accomplished by staff members meeting with the members of the Blue Shield Relations Committee and in turn with each one of the 12 district Blue Shield Relations committees. Personal calls to the physician's office are made in Kansas whenever practicable. Since the Kansas area comprises more than 80,000 square miles with members in all 105 counties, it is necessary to combine meetings whenever possible to conserve the time and energy of busy physicians doing their share of Blue Shield relations work.

The internal case approval section of United Medical Service operates in much the same manner as in Kansas except for the assistance of several physician staff members, both full and part-time The Physicians' Review Committee is composed of a representative physician from each of the 17 county medical societies in the area. At a monthly meeting of this group, all difficult cases and those over which there has been some controversy about the amount allowed, are considered and adjudicated. This is the same service performed by the Review Committee of the Kansas plan. Here, the committee consists of two members of the Blue Shield Executive Committee and one other appointed physician. The parallel between the kinds of cases which need discussion is striking. Operations for cosmetic purposes seem to require much correspondence and discussion in both plans. Occasionally, the amount allowed for unusual and difficult surgery brings a case to the Review Committee just as it does in Kansas.

In setting up a schedule of allowances, the method used in Kansas—that of depending upon a Fee Committee appointed by the president of the Kansas Medical Society—seems to be the favorite approach. At a conference in New York, representatives from all the plans reported on various methods of arriving at equitable fee schedules. The most professional result seems to come from a medical society fee committee, composed of representatives of the different specialty groups. The duty of this committee is to determine the amounts which can be allowed by Blue Shield relating one fee to another, both according to the amount of dues collected and the income levels.

Approval of contracts and forms is the duty of the members of the Blue Shield board in other states, just as it is in Kansas. All plans are continually searching for ways to achieve the greatest results in cooperation between the member, the physician and the plan. Kansas is no different in this respect. Fortunately, the Kansas Blue Shield was the result of foresight on the part of the House of Delegates of the Kansas Medical Society. Each new Blue Shield board faces the problem of continuation of this rapport.

ACTIVITIES OF MEMBERS

Dr. Ray Parmley, Wichita, was a guest speaker at the Southwestern Surgical Congress at Dallas recently, speaking on "Pediatric Anesthesia."

* * *

Dr. C. E. Scott, who practiced in Abilene for four months, has become a member of the staff of the Mowery Clinic in Salina, where he is doing general practice as well as surgery.

* * *

Dr. Irene A. Koeneke, Halstead, was guest speaker at a meeting of the District of Columbia Medical Society last month.

* * *

Dr. L. A. Latimer, Alexander, who retired last month, has announced plans to move to Kansas City, where he and Mrs. Latimer have built a new home. They were guests of honor at a community party at Alexander recently.

* * *

Dr. E. M. Seydell, Wichita, spoke before the Japanese Otolaryngology Society in Tokyo on November 13.

* * *

Physicians who took part in the third annual Reno County Family Institute at Hutchinson recently were Dr. Warren F. Bernstorf, Winfield; Dr.

Edward Greenwood, Topeka; Dr. V. M. Winkle, Topeka, and Dr. John N. Blank, Hutchinson.

* * *

The Bethel Clinic, Newton, announces that Dr. Quentin Cramer is now a member of its staff, specializing in internal medicine. Dr. Cramer is a graduate of the University of Kansas School of Medicine, and recently completed a three-years residency there.

* * *

Dr. R. C. Belisle, Plainville, who has been attached to the First Marine Division for Navy duty, has returned to this country. He is a patient at a Navy hospital in Oakland, California, recovering from injuries suffered in a jeep accident in September.

* * *

Dr. Paul Laybourne, of the University of Kansas Medical Center, spoke at the Atchison County Guidance Clinic recently before clinic board members and home demonstration unit presidents.

* * *

Dr. L. G. Schwartz served as captain of the Community Chest's medical section in Topeka during the fall campaign for funds.

* * *

Dr. Daniel S. Roccaforte, Hanover, who reported for active duty with the air force on November 10, announces that Dr. Robert White, Kansas City, will serve the community during his absence. Dr. Roccaforte expects to serve as a surgeon at the Smoky Hill Air Base, Salina, during his term of duty, and plans to return to Hanover afterward.

* * *

Dr. Funston J. Eckdall of Emporia, Dr. Warren F. Bernstorf of Winfield and Dr. A. E. Hiebert, Wichita, took part in the fall meeting of the Kansas Medical Assistants' Society at Emporia last month. Each spoke briefly at the gathering.

* * *

Dr. Homer Hiebert, Topeka, was one of the speakers at the formal opening of the radioactive isotope laboratory at Hadley Memorial Hospital at Hays last month.

* * *

Dr. Richard Reece returned October 5 from Tokyo, where he had spent a year in Army service, and is now serving again as Butler-Greenwood county health officer.

* * *

Dr. Charles Pokorny, Halstead, was guest speaker at a meeting of nurses of District Four at Halstead, November 11.

* * *

Dr. J. W. Shaw, Wichita, was recently elected president of the Down Town Kiwanis Club in Wichita.

Dr. George Mandeville, Spearville, spoke on medical topics before the Spearville Lions Club at a recent meeting.

* * *

Dr. Robert W. Myers, Newton, who recently returned from service in Korea, showed pictures of activities of the medical corps there before the Woman's Auxiliary to the Harvey County Medical Society on November 3.

* * *

"The Doctor Looks at the Law" was the subject of an address given by Dr. R. M. Gouldner, Wichita, at a recent meeting of the Wichita Bar Association.

* * *

The Turon community and surrounding areas of Reno, Stafford, Kingman and Pratt counties honored Dr. M. S. Thacher, Turon, on November 24. He had completed 50 years of practice in the community.

* * *

Dr. E. Burke Scagnelli, Jetmore, spoke on "Preventive Medicine for the Pre-school and Elementary School Child" at a meeting of the Dodge City P.T.A. on November 13.

* * *

Dr. R. Y. Strohm, Fort Scott, city-county physician, has supervised 2450 "patch" tests for tuberculosis on school children in Fort Scott.

* * *

Dr. C. E. Burtch, Portis, who has practiced 48 years, was guest of honor at a celebration last month on the occasion of his 78th birthday.

The world's weddings, the world's babies and the world's growing population are among the subjects covered in a 700-page volume issued recently by the World Health Organization, "Vital Statistics and Causes of Death."

Marriage rates, according to the report, increased sharply at the end of World War II. Although figures have been decreasing since that time, the number of marriages per year still is higher than the 1936-1938 average.

The increase in the marriage rate was sharply reflected in birth rates, the peak year being 1947. In the United States that year the increase was from 17.2 to 25.8 per thousand. Always in the period immediately following wars there are more boy babies born than girls, and World War II was no exception.

Now is the time to make hotel reservations for the 94th annual session of the Kansas Medical Society, Wichita, May 4-7, 1953.

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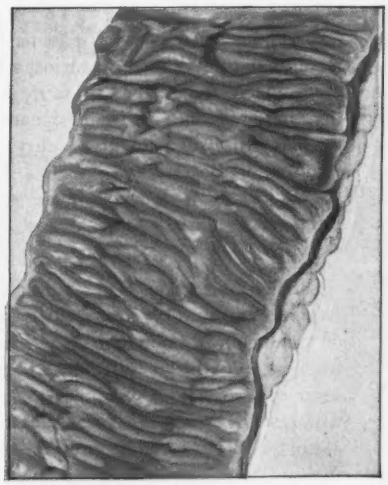
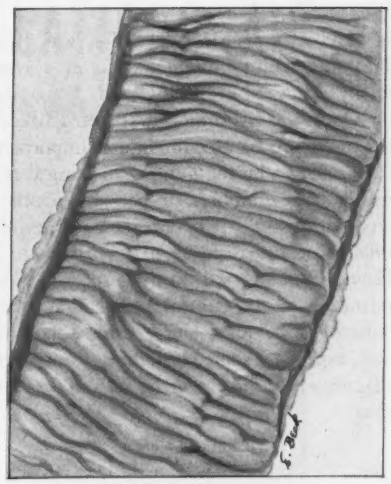


Irritated, injected mucosa such as is produced by roughage.



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* Block, L. H.: Management of Constipation with a Refined Psyllium Mucilloid Combined with Dextrose, Am. J. Digest. Dis. 14:64 (Feb.) 1947.

SEARLE RESEARCH IN THE SERVICE OF MEDICINE

Senior Thesis from the University of Kansas Medical School*
Sarcoidosis

Robert L. Hanes**

Kansas City, Kansas

It is only 16 years since attention was first directed in this country to sarcoidosis as a systemic disease by Hunter in 1936[1] and Longcope in 1937.[2] Once the syndrome was recognized, sarcoidosis proved to be a common and important disorder, as is shown by the number of clinical reports concerning large numbers of patients which have appeared within the last two years, and the increasing amount of literature as to its treatment with ACTH and Cortisone within the last year. A better understanding of the clinical and laboratory manifestations of sarcoidosis, along with certain recent advances, especially some concerning the epidemiology, diagnosis and treatment of sarcoidosis, deserve attention.

Historical Note

The complete history of Boeck's sarcoid has been extensively reviewed by Hunter,[1] and need not be developed in great detail. Nevertheless, a brief review enables one to understand more clearly in what manner the present concept of the disease arose. A factor contributing to the confusion surrounding sarcoidosis is that the varying manifestations of the disease were initially described by various authors as separate diseases. The realization that they were different aspects of the same disease developed only gradually. It is worthy of note, however, that although Boeck appears to have been the first to describe the histologic characteristics of the skin lesions, Hutchinson had already published a clinical description of such a case in 1875. Besnier in 1889 and Tenneson in 1892 had also described lupus pernio, which was later shown to be another skin manifestation of the same disease. The reports following Boeck's in 1899, indicated that other organic systems could also be affected, so that by 1917 Schaumann was able to postulate a generalized disease primarily affecting the lymphohematopoietic apparatus, and only incidentally the skin.[1,3] It is only in recent years (Longcope 1937, Pinner 1938) that such conditions as uveoparotid fever and at least some cases of the Mikulicz syndrome have come to be recognized as special manifestations of the same disease.[2]

Another factor contributing to the early confusion of sarcoidosis, has been the bewildering nomenclature applied to this disease at various times. Fortunately, however, as the disease has been emerging from its status as a medical curiosity and has become more widely recognized as a fairly well defined entity, most of the earlier designations have been gradually discarded in this country in favor of sarcoidosis or Boeck's sarcoid, and benign lymphogranulomatosis (or recognizable modifications of Besnier-Boeck-Schaumann's disease) in Europe.[3]

Etiology

Sarcoidosis remains a disease of unknown cause. At some time or other practically every agent capable of producing a granulomatous reaction or of diffusely affecting the reticuloendothelial system has been suggested as a possible cause of sarcoidosis. The case for tuberculosis was presented in detail in 1946 by Pinner,[4] whose arguments are essentially those of the many other proponents of this theory. Intensive investigation in recent years has failed to yield substantial evidence in support of a tuberculous etiology.[3] Much indirect evidence has been accumulated which argues against a tuberculous etiology, but it must be admitted that this controversy will be convincingly settled only when the cause or causes of sarcoidosis are finally determined.[5]

Pathology

The pathological changes in Boeck's sarcoid are well known and have been reviewed in detail by Freiman[3] (1948). In brief, the basic lesions are granulomatous epithelioid cell tubercles which may completely replace the normal architecture of the organ in which they appear. These tubercles consist of a mass of noncaseating "tubercles" composed entirely of large, pale epithelioid cells with little or no surrounding collar of lymphocytes. Giant cells of the Langhans type may or may not be present. The rare occurrence of peculiar basophilic cytoplasmic inclusions in giant cells has been described.[3] The nature of these bodies and their significance is not known. Although formerly thought to be associated only with sarcoidosis, it was recently emphasized by Riley[6] (1950) that they are nonspecific and occur in other diseases such as leprosy, lupus erythematosis, and occasionally tuberculosis. It is now known that the histologic appearance of the lesions, even in clinically typical cases, is subject to some variation. Even the characteristic absence of necrosis is not constant; small necrotic foci in the central portions of the lesions have often been described and are no longer considered incompatible with the diagnosis.[3] Moderate numbers of lympho-

*This is one of 11 senior theses selected for publication by the Editorial Board from a group of 15 judged the best by the faculty of the University of Kansas School of Medicine.

**Senior Student, University of Kansas School of Medicine.

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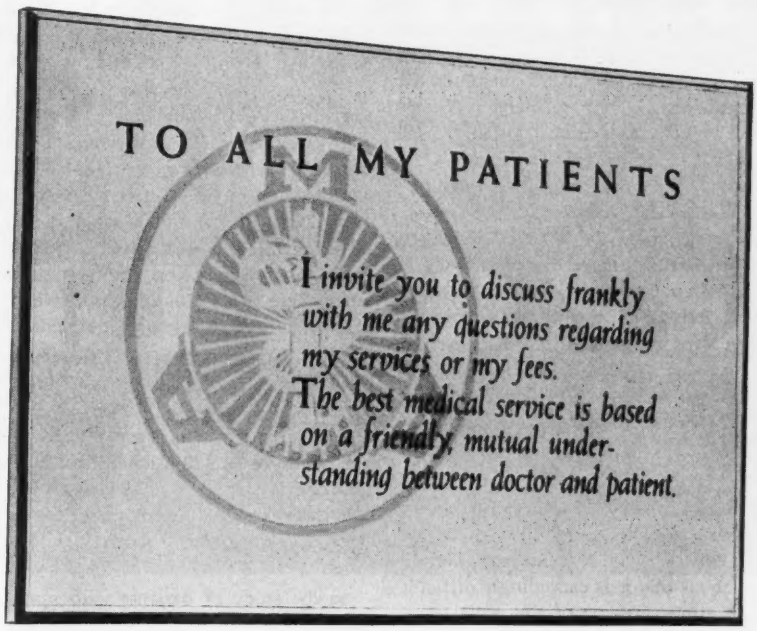
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cytes may be scattered among the epithelioid cells, but neutrophils and eosinophils are practically never present. Giant cells are frequently not prominent, but their rarity is not a dependable diagnostic point as was once thought.[6]

It is important to remember that sarcoidosis is a systemic disease and the discovery of epithelioid tubercles in excised surgical specimens does not establish a diagnosis of sarcoidosis, unless there is clinical or roentgenologic evidence of involvement elsewhere. Isreal and Sones (1952),[5] have encountered several instances in which typical sarcoid lesions were detected in isolated lymph nodes and in which prolonged observation has demonstrated no evidence of systemic involvement. Nadel and Ackerman, 1950,[7] have reported five cases in which lymph node changes characteristic of sarcoidosis were observed in association with neoplasms. This demonstration of the nonspecific character of the sarcoid granuloma emphasizes anew the fact that the diagnosis of sarcoidosis requires more than a pathologic report of sarcoid tubercles.

Riley, 1950,[6] feels that the term sarcoidosis should be reserved for the generalized disease with evidence of widespread disseminated foci in which there must be a close correlation between the clinical findings and the evaluation of pathologic material.

Incidence

The distribution of sarcoidosis seems to be world wide. More cases have been reported from the Scandinavian countries, Canada, and the United States. Freiman[3] feels that it is exceedingly difficult to make even an approximation of the actual incidence, as a fair number of probable cases have never been confirmed, and still others have most certainly been overlooked.

It is now generally agreed that, in this country at least, the disease appears most frequently in the Negro race.[3,8,9] Recently, Michael (1950)[8] surveyed 350 cases with special reference to epidemiology. The rate in southern Negroes was 15 times that in northern born Negroes; the rate in southern whites was six times that of northern born whites, and was higher than that of northern born Negroes. A somewhat similar observation had been made several years earlier by Tornell in Sweden, who had remarked on the frequency of an agricultural background in his patients with sarcoidosis, and had suggested on the basis of this association the likelihood of a mycotic etiology of the disease.[8]

Isreal and Sones (1952)[5] emphasize that sarcoidosis appears to be extremely rare among what is the largest group in this country, the native born urban white. They further state that this fact is of diagnostic value; caution should be exercised before making a diagnosis of sarcoidosis in patients not of southern or rural origin.[5] This observation suggests either an infectious agent prevalent chiefly in this country in the rural south, or some constitutional or environmental abnormality occurring in childhood years resulting in a modification of response to irritants or infection in later years.[5] In any event, no theory of the etiology of sarcoidosis can be seriously entertained that is not in accord with these geographic facts.

Symptoms

The manifestations of this disease are many and varied because of the number of organs and tissues which may be involved. McCort (1947),[10] recognizes four clinical types as they present themselves to the physician. These are: (1) the sarcoids of the skin as described by Boeck and Besnier, (2) the uveoparotid fever of Heerfordt, (3) the type with lymphadenopathy of superficial or intrathoracic nodes simulating lymphoblastomas, and (4) a type in which there is primarily involvement of the pulmonary parenchyma on roentgen study and which, when there is also cough, loss of weight, and slight fever, may closely resemble pulmonary tuberculosis.

The majority of symptoms, as reported by numerous authors, appear to be referable to the chest, which is not surprising if the high incidence of pulmonary involvement is considered.[3] Riley 1950,[6] lists sputum, cough, weight loss, and weakness as the four most numerous symptoms in that order of frequency in his recent series of 52 patients, which closely corresponds with that of numerous others.[3,9,10]

In the study of patients with sarcoidosis, one is impressed by the fact that symptoms, when they exist, are caused primarily by mechanical interference with the function of organs rather than by any form of intoxication. When the miliary "hard tubercles" collect in great numbers, they tend to displace or destroy normal tissue or may even produce tumor-like masses that involve one or several organs. In certain organs, such as the skin and the superficial lymph nodes, this growth of sarcoids causes little or no damage, but in the eye, the mediastinum, the lungs, or in rare instances, the central nervous system and the heart, the accumulation of sarcoids may produce great destruction or actually cause death.[3,10]

Clinical Observations

One is referred to Freiman's recent review of the literature which gives an extensive discussion on the involvement of systems and individual organs. No such elaborate review will be given here. However, the most constant findings deserve mention.

Involvement of the lymph nodes as manifested by palpable or roentgenographic enlargement is demonstrable in almost every case.[6,9] The intrathoracic nodes appear to be the group most consistently

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affected, and in almost all cases have shown prominent hilar shadows. The enlargement is usually bilateral, as distinct from tuberculosis, which is usually unilateral. The nodes have little tendency to coalesce; even considerable enlargement of the hilar nodes is rarely associated with pressure or other obstructive phenomena.[3] Peripheral lymph-adenopathy is the next most frequent finding and was noted in 60 per cent of Riley's patients, most usually generalized and only rarely limited to a single node or to one or two groups.[6]

Involvement of the pulmonary parenchyma is often a prominent feature of the disease. The roentgenographic pattern is by no means pathognomonic and may be mimicked by a wide variety of conditions. The infiltrations tend to be diffuse and bilateral, but may be localized in certain phases. The roentgenographic appearance of the chest is largely dependent upon the phase of evolution of the disease at any given time, and a number of authors have had the opportunity to follow the phases of development and regression of such lesions with serial roentgenograms. Early lesions tend to be of the miliary or nodular disseminated type. They are in large measure reversible and may resorb, leaving little or no trace. The linear, strand-like type lesion may also resorb partially or completely, but shows a greater tendency to fibrosis. With the onset of interstitial fibrosis, complete resorption is no longer possible.[12]

Hepatomegaly and splenomegaly are the next most frequent manifestations.[6] In spite of the frequency of liver involvement, Shay (1951)[13] has shown that liver function rarely seems to be significantly disturbed.

Involvement of the eye and its related structures is reported in 25 to 50 per cent of cases in recent series.[6,8,9] These figures are substantially higher than older estimates and clearly represent the now general acceptance of the uveoparotid syndrome as a manifestation of sarcoidosis.[6] Eye involvement usually manifests itself as a painless iritis or iridocyclitis, either bilateral or, less commonly, unilateral. Although the lesions may resorb completely, such serious complications as posterior synechiae, corneal opacities, and phthisis bulbi have been frequently observed.[6,9]

The incidence of roentgenographically demonstrable bone involvement ranges from 15 to 25 per cent of cases as shown by Freiman's review.[3] The osseous lesions show a predilection for the phalanges and when demonstrable are of diagnostic significance, although lesions have appeared in the long bones and elsewhere. These changes have recently been reviewed by Holt and Owens,[14] and consist essentially of two types. The first type consists of well localized punched out cystic areas without evidence of surrounding inflammatory reaction. The second type, considered more characteristic of sarcoidosis, consists of marked alteration in the trabecular structure of the bone with extensive cortical atrophy and resorption. Pain is conspicuously absent.[14]

Laboratory Findings

Perhaps the most consistent of all the laboratory observations in this disease is the reaction to the tuberculin skin test, which in a great majority of instances is negative. Most estimates of the incidence of such nonreactors range between 60 and 70 per cent of the cases, the remaining positive cases usually tending to be weak.[5,6,9] Isreal and Sones[15] have recently shown that the majority of these patients with sarcoidosis failed to develop tuberculin sensitivity following B.C.G. vaccination. A similar response to B.C.G. vaccination has been reported in patients with Hodgkin's disease, and presumably in both diseases represents a general and non-specific immunologic impairment.[15]

Another interesting and significant symptom, when present, is the elevation of the globulin fraction of the blood protein, which occurred in 70 per cent of patients in recent series.[6,9] The rise in globulin may occur at the expense of the albumin, so that reversal of the ratio may be observed even in cases in which the total protein shows little or no increase.

Other inconstant findings include mild leukopenia, monocytosis, and eosinophilia, but they carry little diagnostic significance.[10] Elevations in serum calcium with values as high as 100 mg. per 100 cc. have also been noted. Hypercalcemia, when it does occur, is often associated with hyperglobulinemia, and some relation between the two has been suggested on the basis of the calcium-binding power of serum protein.[3] The skin test for sarcoidosis, known as the Kveim reaction, has found little diagnostic use in this country due to its slow reaction, long duration of the lesion produced, and occasional severity of the lesion produced.[10]

Treatment

Without a true knowledge of the cause of sarcoidosis, all methods of treatment are entirely empiric. Various arsenicals, leprosol, tuberculin, x-ray, radium, ultra violet rays, urethane, and streptomycin have all been employed with equivocal results.[3] Recently, however, more consistent, dramatic improvement has been obtained with ACTH and cortisone. Stone,[16] 1951, followed shortly by Siltzbach,[17] Lovelock,[18] and Small,[19] recently reported most favorable results with cortisone in sarcoidosis.

Siltzbach, February, 1952,[20] has reported on the largest series of patients, all 31 of whom showed

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marked subjective and objective improvement while on cortisone therapy. The course of cortisone therapy in his series ranged from four to 15 weeks. The daily dose was 100 to 150 mg. Fresh lesions seemed to be more amenable to therapy than older ones, although lesions known to have existed as long as two years also proved responsive. Regression of peripheral lymphadenopathy, pulmonary parenchymal lesions, osseous lesions, skin lesions, and eye lesions were demonstrated following two to four weeks of therapy.[20]

The response to cortisone was irregular and often transitory. In the same patient some sites regressed while others remained refractory, but in no patient could progression of lesions be detected.

Isreal and Sones[5] have treated 10 patients with cortisone and have noted similar dramatic improvement. In one case there were cutaneous, ocular, pulmonary and lymph node lesions. Marked regression occurred at these sites after a 15-day course using 200 mg. of cortisone daily. Biopsies of a cutaneous lesion and a peripheral lymph node at the end of the course showed complete replacement of the sarcoid granulomas by non-specific inflammatory tissue. Chest films three months later showed no recurrence of pulmonary nodular lesions or mediastinal lymphadenopathy. Transient improvement was noted in five patients with disease of long standing. It is their belief at present that treatment with cortisone is indicated in patients whose sarcoidosis appears to be recent and fresh. Treatment does not appear to be warranted in patients with chronic sarcoidosis and few symptoms, while a trial of these drugs is advisable in patients with ocular lesions, with pulmonary insufficiency, or other manifestations of progressive disease.[5]

It has recently been my privilege to observe a patient at the Kansas University Medical Center, who presented ocular, pulmonary, and peripheral lymphadenopathy lesions of sarcoidosis. This patient was initially started on 200 mg. of cortisone daily, which was reduced to 150 mg. on the third day and to 100 mg. daily on the sixth day. Local treatment to the eyes consisted of cortisone opthalmic drops (1.5 per cent solution). Therapy continued for 22 days, at which time the patient was gradually taken off cortisone therapy as recommended by Lovelock,[18] who feels that gradually diminishing doses of cortisone tend to reduce the relapse rate. Marked, dramatic improvement was noted in the ocular lesions, with alleviation of the iridocyclitis and with marked improvement in vision following only one week of therapy. Clearing of the lungs, with complete resolution of the peripheral lymphadenopathy was noted both clinically and with serial roentgenograms and biopsies. This marked improvement was thought to be significant, and did not represent a spontaneous remission of sarcoidosis. This patient has not been followed for a sufficient period of time to note any relapse.

Decisive evidence that the natural course of the disease is fundamentally affected by the use of cortisone is lacking; yet the repressive effect of the drug appears to be of value in reducing the activity of lesions and minimizing the damage to vital organs during exacerbations of the disease.[20] For the present it would seem wise to use cortisone particularly in those cases in which the site and extent of involvement portends dire consequences to the patient.

Prognosis

The Scandinavian use of the term "benign lymphogranulomatosis" for this disease and some of the earlier American reports on sarcoidosis have given a falsely sanguine impression concerning the course of this disease. It was considered at one time that except for the risk of development of tuberculosis, sarcoidosis was almost invariably benign. Isreal and Sones,[5] in their recent follow up of 59 patients for a mean interval of more than four years, report a mortality rate of 12 per cent. One of the deaths was from tuberculosis; the remainder were due to respiratory insufficency resulting from sarcoidosis. This finding is consistent with that of Riley,[6] who reports a mortality rate of 20 per cent. It is clear that prolonged observation will be necessary before a balanced view of the prognosis will be acquired, but these initial findings suggest that superinfection with tuberculosis is less frequent than has been reported, and that sarcoidosis is in its own right much more malignant than has been recognized.

Summary

A review of the pertinent literature on sarcoidosis has been presented with emphasis on recent advances in both diagnosis and treatment. Sarcoidosis remains a disease of unknown cause. Considerable confusion has resulted in the past from the assumption that the morphologic appearance of the lesion is pathognomonic. A wide variety of agents, of which the unknown cause of sarcoidosis appears to be only one, seem capable of inducing the characteristic granuloma, and it has become increasingly clear that a careful distinction must be made between the term "sarcoid lesion" and the disease "sarcoidosis." The frequency of a southern, rural background of patients in this country has been observed and appears of diagnostic significance. Marked, dramatic improvement has been noted following treatment with cortisone. It is too early to completely evaluate the use of cortisone in sarcoidosis, but it appears to be of value in recent and fresh cases and is especially warranted when lesions locate in vital organs. Recent findings suggest that sarcoidosis is in its

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*Nutrients for which daily dietary allowances are recommended by the National Research Council.

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New Heart Device at K.U.

A new device developed at the University of Kansas Medical Center by Dr. E. Grey Dimond, director of the cardiovascular laboratory, will make possible the transmission of heart tracings by telephone, cable or radio telephone. It is called the "Tele-EKG."

Electrical impulses representing the action of the patient's heart are taken directly from the patient's body, fed to the telephone line, and are reproduced in chart form in the specialist's laboratory. Thus, a heart patient could have his ailment diagnosed by a specialist hundreds of miles away without delay.

In the initial demonstration, an electrical tracing of the heart action of a patient at the student hospital at the University of Kansas campus in Lawrence was transmitted to Doctor Dimond's laboratory in Kansas City. Next April the unit will be demonstrated between Kansas City and Atlantic City, where the American Heart Association will be meeting.

Development of the device was financed by the National Heart Institute. Dr. Dimond was assisted in producing the unit by Mr. Fred Berry, of the medical center's electronics laboratory.

ANNOUNCEMENTS

The Institute of Industrial Health of the University of Cincinnati will accept applications for a limited number of fellowships offered to qualified candidates who wish to pursue a graduate course of instruction in preparation for the practice of industrial medicine. Requests for information may be addressed to the Institute, College of Medicine, Eden and Bethesda, Cincinnati 19, Ohio.

* * *

The 9th annual clinical conference of the Chicago Medical Society will be held March 3-6, 1953, at the Palmer House, Chicago. A faculty of more than 35 outstanding speakers will take part in the program, and another group will give daily teaching demonstrations which will include the presentation of patients. They will emphasize the technique to be employed in handling orthopedic, medical and pediatric problems. Panel discussions at round table luncheons will also be featured. In addition, there will be technical and scientific exhibits.

Physicians who are not members of the Chicago Society may attend by paying a registration fee of $5.00.

* * *

The Sixth Pan-Pacific Surgical Congress will be held in Honolulu in November 1954. Physicians in this country wishing to attend may secure details from the Pan-Pacific Surgical Association, Suite 7, Young Building, Honolulu, Hawaii.

A suggestion that female sex hormones may be the key to the mystery of why women under 50 are far less susceptible than men to hardening of the coronary arteries was made recently by Dr. Jeremiah Stamler, Michael Reese Hospital, Chicago, before the Council for High Blood Pressure Research of the American Heart Association.

As a result of laboratory experiments with chicks, Dr. Stamler drew the tentative conclusion that estrogen made the so-called "weaker sex" less apt to develop hardening of the coronary arteries before the menopause period. In contrast, however, atherosclerosis that developed in the aorta proceeded without interruption, despite estrogen. On the basis of this finding, Dr. Stamler suggested that research workers experimenting in this field cannot confine their studies to the aorta.

He reported also on the varying effects obtained when different hormone secretions of the adrenal cortex are administered to laboratory chicks. He believes that the ratio between the concentration of cholesterol and of phospholipids in the blood may be a significant factor influencing coronary atherosclerosis.

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COUNTY SOCIETIES

A meeting of the Central Kansas Medical Society was held at Hays on October 16. Dr. R. H. Maxwell, Wichita, spoke on "Caesarean Section" and Dr. C. M. White, Wichita, discussed "The Detection and Interpretation of Pathology in the Upper G. I. Tract."

* * *

The Sedgwick County Society met on November 5 to hear a program presented by the Cancer Committee of the Society, under Dr. H. W. Brooks, chairman, and Dr. H. C. Blaylock, co-chairman. Dr. C. T. Hagan spoke on medical aspects, Dr. John Kline on radiological aspects and Dr. W. P. Callahan, Jr., on pathological aspects of "Malignancy of Transverse Descending Colon, Sigmoid and Rectum." Discussants were Dr. John Fulton, Dr. R. E. Hines and Dr. James Holt.

* * *

Dr. Warren F. Bernstorf, Winfield, president of the Kansas Medical Society, and Mr. Oliver E. Ebel, Topeka, executive secretary, were guest speakers at a meeting of the Cloud County Society held November 6 in Concordia.

* * *

A joint meeting of the Nemaha County Medical Society and Auxiliary was held at the home of Dr. and Mrs. C. M. Barnes, Seneca, on October 28. After a buffet supper, the physicians held a business meeting and viewed a medical film.

* * *

Dr. John P. White, Parsons, was named president of the Labette County Society for 1953 at a meeting held last month at the Parsons Country Club.

* * *

Dr. and Mrs. Louis Graves, St. John, entertained members of the Stafford County Society and Auxiliary at a dinner at their home on October 13. Separate business sessions were held later in the evening.

* * *

A meeting of the Doniphan County Society was held recently and Dr. Robert Corder, Highland, was named president for 1953. Dr. Emerson Yoder, Denton, was elected vice president.

* * *

A meeting of the Shawnee County Society was held at the Hotel Jayhawk, Topeka, on November 4. Speaker of the evening was Dr. Maurice B. Strauss, Boston, who discussed "Pernicious Anemia, Vitamin B-12 and Folic Acid."

* * *

Three county societies, Sumner, Harper and Barber, made plans for merging into a Tri-County Society at a meeting held at Harper on November 19. Dr. Warren F. Bernstorf and Mr. Oliver E. Ebel, president and executive secretary, respectively, of the Kansas Medical Society, were present for the organization meeting. The following officers were elected: president, Dr. L. C. Joslin, Harper; vice president, Dr. J. D. Hilliard, Medicine Lodge; secretary-treasurer, Dr. Albert C. Hatcher, Wellington.

Technical Report on Blood

Publication of a complete and authentic report on blood, "Standard Values in Blood," was announced recently by the United States Air Force. Information for the publication was contributed by more than 600 leading medical authorities throughout the world.

The report was prepared by the National Research Council under sponsorship of the Aero Medical Laboratory. Dr. Errett C. Albritton, of the George Washington University Medical School, served as editor.

Data included in the more than 100 tables in the report describe practically every known property of blood. Each of the thousands of individual figures was verified at least six times, and some of them were rechecked as high as 20 times. The report includes chemical and biological properties of blood, latest knowledge on coagulation, blood groups, and the effective blood levels of various drugs and therapeutic agents.

Among the interesting facts revealed in this study is that blood contains more than 300 chemical compounds ranging from complex hormones, enzymes and vitamins to simple metallic elements such as copper, zinc, manganese and iron.

Copies may be secured from the Office of Technical Services, Department of Commerce, Washington, D. C.

The accurate reporting of medical news is a service to which the public is entitled. However, inaccurate reporting of medical news, even though it is unintentional, is definitely a disservice and cannot help but disturb and disrupt the high-level relationship that has been cultivated for many years between the doctor and the patient, and between the pharmacist and the patient—extremely valuable relationships which build for mutual confidence and respect all along the line in the health professions. —*Graydon L. Walker, Parke, Davis and Company.*

Telepaque, the new radiopaque medium for gallbladder visualization introduced by Winthrop-Stearns, Inc., is credited as opening a new field in study of the biliary system by Dr. William H. Shehadi of the department of radiology of the New York Polyclinic Medical School and Hospital.

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BOOK REVIEWS

The Prenatal Origin of Behavior. By Davenport Hooker. Porter Lecture Series 18. Published by the University of Kansas Press, Lawrence, Kansas. 143 pages. Price $2.50.

This book comprises the 18th series of Porter Lectures given at the University of Kansas.

The first chapter reviews the observations on the fetal activity of infrahuman vertebrates from the classical work of Coghill up to the present time. Coghill's concept maintains that reactive behavior starts as a total pattern in which neuromuscular mechanisms capable of functioning participate from the beginning, and this pattern is expanded as more mechanisms become functional. New neural elements integrate with those already functioning. Local reflex patterns become engrafted on the total pattern in a cephalocaudal and proximodistal direction.

Apposed to this view is the concept of Swenson and Windle in which behavior is assumed to develop by the appearance of a localized, nonintegrated, unitary response, upon which others become secondarily integrated. Windle thinks that anoxia in the fetal blood soon induces abnormal responses. The sequence of development of activity in the human fetus is described in the second chapter. The author has taken an active part in the investigations on human fetuses. The third and last chapter considers the structural and functional interrelationships in prenatal activity.

Evidence gathered appears to indicate that behavior of vertebrates, including man, has its genesis in the early exteroceptive responses exhibited during embryonic, larval, or fetal life. Although there is some similarity in the succession of responses to external stimuli in the vertebrate series, the various classes of vertebrates have their own individual characteristics in the development of behavior. Voluntary acts, when they appear, develop upon the earlier reflexogenic sequences of prenatal life. This book demonstrates a contribution that pure science in the field of morphology can contribute to the large problem of behavior. It should be of interest not only to anatomists but also to workers in other disciplines dealing with the problem of behavior.—*A.T.S.*

* * *

Therapeutic Meal Plans—A New Diet Manual. By Virginia Toews, Berdena Rosenow and Ruth Gordon. Published by University of Kansas Press, Lawrence, Kansas. 111 pages. Price $3.00.

This manual is a well organized, complete guide for those persons concerned with dietary treatment. The meal plans as described are thorough and accurate. The food lists are complete and the diets explained simply. The additional pamphlet in the back of the book which lists diets for pathological conditions would be most helpful, particularly to house staffs.

The book is compact and printed with no wasted space, one diet followed closely by the next. This might initially confuse the inexperienced; however, the manual is so well indexed that it should cause no serious difficulty.

* * *

Brain Surgeon—The Autobiography of Dr. William Sharpe. Published by The Viking Press, Inc., New York, New York. 271 pages. Price $3.75.

This book presents in easily readable form the medical and social reminiscences of one of the pioneer neurosurgeons in New York City. The author's interest in Pan-American medicine, cerebral palsy and racial equality dominates throughout. While many will not agree with the neurosurgical opinions expressed herein, those interested in the early development of neurosurgery will find an enjoyable evening's reading in this book.—*C.E.B.*

* * *

The Treatment of Injuries to the Nervous System. By Donald Munro. Published by W. B. Saunders Company, Philadelphia. 284 pages, 46 illustrations, 7 tables. Price $7.50.

Written primarily for the general surgeon and general practitioner, this book covering the injuries to the nervous system is essentially a revision of the author's former publication on cranio-cerebral injuries with the additional inclusion of consideration of injuries to the spinal cord and peripheral nerves.

The cranial injuries are first considered with attention to general problems of head injuries and the operative and non-operative treatment. It is difficult to agree with the author's advocacy of critical lumbar puncture, and many neurosurgeons would not agree that tracheotomy is contraindicated in severe head injuries. The author also considers cranio-cerebral injuries in children, newborn, and a very complete consideration of injuries to the spinal cord and their consequences is presented.

Very brief presentations of peripheral nerve and autonomic nervous systems are also given, along with useful brief chapters on the cost of medical care of these injuries and rehabilitation considerations.

The book is well-written and easy to read, and appears to accomplish its purpose in forming a reference guide for the surgeon and general practitioner handling these injuries.—*C.E.B.*

* * *

Pharmacology in Clinical Practice. By Harry Beckman. Published by W. B. Saunders Company,

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ISODORE LAMPE, M.D., Department of Roentgenology, University Hospital, University of Michigan, Ann Arbor.
SIMEON T. CANTRIL, M.D., Tumor Institute, Swedish Hospital, Seattle, Wash.
DAVID PUGH, M.D., Section of Diagnostic Roentgenology, Mayo Clinic, Rochester, Minnesota.

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Errors in Gastro-Intestinal Diagnosis
Polyps of the Colon
Roentgen Aspects of Arthritis
Value of Study of the Spine in Anterior, Posterior and Lateral Bending
Hemorrhage of Upper Gastro-Intestinal Tract of Undetermined Origin
Intestinal Ileus
The Purged Colon
Melorheostosis Leri
Influence of Genotype and Endocrine Factors on Bone Development—Clinical, Roentgen and Isotope Appraisal
Metabolic Bone Diseases
Aseptic Necrosis
Benign Bone Tumors
Tumors of the Jaw
Beta Radiation of the Eye
Results of Treatment of Carcinoma of the Lip
Treatment of Cancer of the Larynx from Standpoint of Radiation Therapy
Radiation Therapy of Breast Carcinoma
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Philadelphia. 839 pages, 152 figures. Price $12.50.

This textbook, which is the latest one to appear on pharmacology, is an entirely different approach to the subject than that found in other available texts on the subject. In many respects it is like the author's well-known "Treatment in General Practice."

On the premise that the doctor at the bedside reasons from "the patient and his malady" to the drug and not in the reverse order, the author has approached the subject from the standpoint of diseases and their treatment. Except for a few chapters in which a group of drugs is treated as a unit, the arrangement of material is according to disease states, and all useful drugs employed in the treatment of a given condition are located under one chapter heading.

The book is comprised of two sections. Section I deals with the pharmacologic aspects of drugs used in various diseases; Section II offers a brief resume of the chemical and physical characteristics of the drugs considered in Section I.

While by no means exhaustive, the book covers the array of drugs useful to the medical profession. The reviewer would definitely like to see an expansion of the discussions on basic principles of pharmacodynamics in future editions; and, although he will agree with the author that much of the subject of structure-activity relationship is not required by the undergraduate medical student, feels that a minimum amount of instruction is necessary for a fundamental understanding of pharmacology.

As a reference for the practicing physician, the text can be heartily recommended as a lucid and up-to-date presentation of the subject in the pleasant informal style characteristic of the author's writings. For the undergraduate medical student it is recommended as supplementary, rather than as the sole textbook for a course in pharmacology.—*R.E.G.*

ABSTRACTS FROM CURRENT LITERATURE

Primary Atypical Pneumonia in Children

Treatment of Primary Atypical Pneumonia in Children with Aureomycin. By Charles E. Anderson. Am. Jnl. Dis. Child., 80:4, 533-540, Oct., 1950.

There may be a synergism between streptococci and some unknown virus in the causation of this disease.

Diagnostic criteria are: (1) gradual onset, nonproductive cough and fever, cough increasing and worse at night; (2) minimal chest signs, much less than one would expect to find with actual consolidation; (3) laboratory findings showing low to normal leukocyte count; (4) serologic studies on serial sputum specimens do not reveal the development of antibodies for recognized viral or rickettsial agents. (5) treatment with sulfa or penicillin does not produce improvement in the uncomplicated case; (6) the appearance in the serum of patients of cold agglutinin for the human group 0 cells or agglutinins for streptococcus M G during the course of the disease or in convalescence.

The author reports a group of 19 children, all of whom had typical infection of the upper respiratory tract with cough, roentgen evidence of pneumonitis, leukopenia in most instances, and invariable increase in lymphocytes. All patients were given two to three days trial with penicillin or sulfa, despite which therapy they were clinically worse or unimproved. With one exception, the roentgen manifestation of disease was a rather fan shaped infiltration in the bases of one or both lungs. There were no complications of any kind in this series of cases.

Treatment other than use of aureomycin included only steam, aspirin and syrup of dihydrocodeinone bitartrate for the nocturnal cough.

Cough persisted 5.4 days; roentgen findings persisted 5.7 days.—*D.R.D.*

* * *

Propylthiouracil in Thyrotoxicosis

Propylthiouracil in Thyrotoxicosis: Alternate Cases Treated Medically and Surgically. By Nelson Taylor, Alfred Large and Paul Noth, Am. Jnl. Med. Sc., 220:4, 362-372, Oct., 1950.

A series of 52 cases was studied in sufficient detail over a two-year period to warrant reporting. The cases of diffuse goiter with hyperthyroidism were treated alternately by surgical and medical techniques. Very few of the cases in either series represented uncomplicated hyperthyroidism, cardiac complications being most commonly present. Average initial basal metabolic rates were high, between 55 and 60 per cent.

Of 20 cases of diffuse goiter treated surgically 16 were followed sufficiently to justify conclusions. Thirteen of these obtained sustained remission without further therapy. Three required thyroid extract for postoperative hypothyroidism. Preoperative propylthiouracil was used.

Of 21 cases of diffuse goiter treated medically with propylthiouracil, only 12 cooperated and could be followed. Only three of these obtained sustained remission without further therapy. Nine were still receiving propylthiouracil at the time of the report. The actual duration of treatment to produce an expected remission is not clearly stated.

Six of seven cases of nodular goiter with hyperthyroidism were followed adequately after surgical

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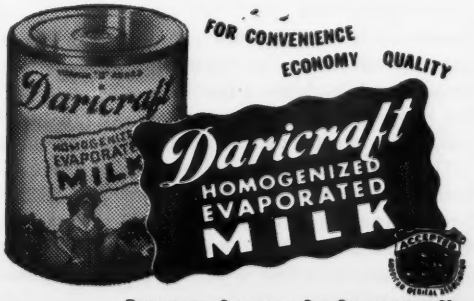

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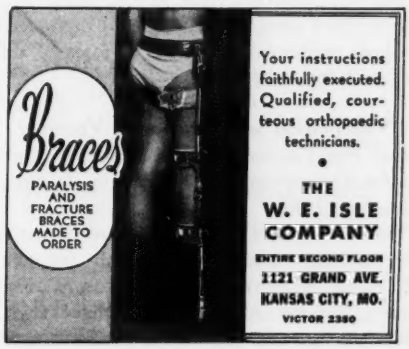

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treatment. All obtained sustained remissions. Preoperative propylthiouracil was used.

Three similar patients were followed under medical management with propylthiouracil. Two were still receiving the drug at the time of the report. One died of gastrointestinal hemorrhage, not apparently related to the drug.

There was no mortality from treatment in either the medical or surgical group. One case of agranulocytosis occurred, but was treated with penicillin and subsided.

A significant increase in exophthalmos occurred in 8 of 52 patients while receiving propylthiouracil. No significant progression of exophthalmos occurred in any case postoperatively, and definite regression occurred after thyroidectomy in four cases.

The authors conclude that subtotal thyroidectomy is still the treatment of choice in cases of diffuse goiter with hyperthyroidism.—*E.J.R.*

* * *

Vaccination with Prolonged Vaccinia

Small Pox Vaccination with Prolonged Vaccinia. By John A. Bigler and Eugene Slotkowski, Ped., 7:1, 24-33, Jan., 1951.

There are reports in the literature of extremely severe primary reaction take, with and without death. Cases of xeroderma pigmentosum (Kaposi's disease) and vaccinia vaccinatum have also been reported frequently. In these, death occurred or the disease ran a self-limited course with all the lesions in the same stage.

Author's Summary: Definite clinical, histological and immunologic changes take place following smallpox vaccination. After its full development on the ninth or tenth day, the vaccinial lesion is followed by drying, crusting and scarring. Histologically, there are degenerative and irritative changes in the epidermis believed to be due to the direct action of the virus on the epithelial cells. Immunologically, humoral antibodies to vaccinia begin to appear at the end of the first week following cutaneous vaccination, increase in amount during the second and third weeks, and reach a maximum at the end of the third week. The probable reason for the involution of the vaccinial lesion after the pustular stage is the appearance of specific antibodies in the blood which apparently neutralize the vaccinia virus. The presence of histologically active vaccinial lesions approximately four months after implantation of the vaccinia virus could be explained only on the inability of the child to develop immunity to the vaccinia virus. Because of this lack of immunity, degenerative action of the vaccinia virus continued unopposed.—*D.R.D.*

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Isolation of ACTH

The isolation of pure adrenocorticotrophic hormone, ACTH, was announced last month by F. W. Specht, president of Armour and Company. The feat was achieved by a team of six chemists who have worked intensively for more than three years on the project.

ACTH was first introduced for medical use by the Armour Laboratories in 1949. Since then it has been used in the treatment of many complex diseases such as arthritis, asthma, allergy, rheumatic fever, nephrosis, and others.

Pure ACTH is described as a white powder soluble in water. It is a protein with a molecular weight of about 3,500, much smaller than originally estimated, and appears to consist essentially of a single chain of amino acids. It has 150 to 200 potency units per milligram.

In addition to providing a firm standard against which to measure therapeutic preparations of ACTH, the pure substance opens the way to research on the underlying mechanisms by which the hormone exercises its remarkable effects in protecting against the shock of disease, poisoning or other damage to body cells.

Because its therapeutic effects are exactly the same as those of ACTH, the pure product will not be put on the market, but will be made available for research.

List of Medical Films Available

A new revised film list, including 78 medical films not readily available from other sources, has been published by the Committee on Medical Motion Pictures of the A.M.A. Copies may be obtained from the committee, A.M.A. Offices, 535 North Dearborn Street, Chicago 10, Illinois.

Helicopter ambulance units, designed to evacuate critically wounded patients from forward combat areas, have been authorized as an integral part of the organization of the Army Medical Service in the theater of operations, the Department of the Army announced recently.

Helicopters have been used since early in the Korean conflict to rush severely injured soldiers from battalion aid stations or regimental collecting stations to mobile Army surgical hospitals and rear-area evacuation hospitals, but they have not previously been incorporated in formal field-type units.

The first helicopter ambulance unit is being activated at the Medical Field Service School, Fort Sam Houston, Texas, where it will be used for training purposes. Additional units will be formed in Korea and elsewhere as personnel and equipment become available.

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Gallbladder Surgery, Ten Hours, starting April 20.
Surgery of Colon & Rectum, One Week, starting March 2.
General Surgery, One Week, starting February 9.
General Surgery, Two Weeks, starting April 20.
Fractures and Traumatic Surgery, Two Weeks, starting March 2.

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Committee Chairmen for 1953 Meeting

Dr. Howard C. Clark, president-elect of the Sedgwick County Medical Society, has announced the appointment of the following committee chairmen for the 1953 annual meeting of the Kansas Medical Society, to be held in Wichita, May 4-7, 1953:

General Chairman—Dr. Edward S. Brinton
Scientific Program—Dr. James B. Fisher
EENT Program—Dr. Norton L. Francis
Entertainment—Dr. Lester K. Nix
Reception—Dr. Lloyd P. Warren
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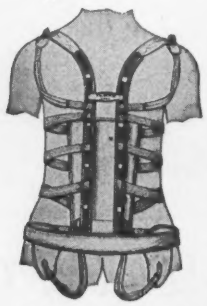

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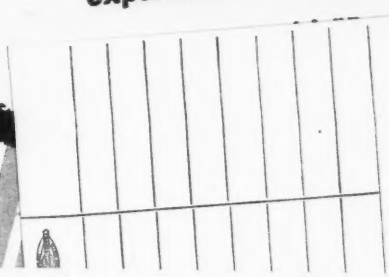

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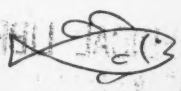

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